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## Original Communications

### INFANTILE ECZEMA


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## Section I

### Classification, Etiology, and Pathogenesis

There is no common disorder which is more difficult to see clearly than infantile eczema. One of the principal reasons for this is that the broad group which we call "eczema" is composed of a number

Fig. 1.—Eczematous face, showing punctate appearance.

of probably unrelated conditions, and clarity can never result until we are able to resolve the group into its component parts.

It is not possible at present to do this with hard and fast lines, but it is possible to do so in a general way, on a purely clinical basis, according to what one sees in the patient. Such a division, imperfect as it is, makes a beginning. Moro[1] recognizes three groups which are ordinarily included under the term "infantile eczema," each one of which has certain fairly definite characteristics, and I believe that if this division is followed, much will be gained.

It may be that these three clinical conditions represent entirely different diseases, but they so overlap, and so many mixed forms are seen, that it is not possible at present to be sure of this.

1. *Seborrheic Dermatitis.*—This consists of inflammatory redness and scaling, most often seen on the scalp, face, back, and chest. The scales may be white and dry, or yellow and greasy. The process is not as a rule moist, and does not have the characteristic vesiculation of true eczema. It often occurs in rather sharply circumscribed patches, and not infrequently has a close resemblance to psoriasis. Skin tests to proteins are not so likely to be positive as in true eczema, and itching is not so severe. It is not so resistant to treatment, and often yields remarkably well to tar, sulphur, or ammoniated mercury—all anti-

Fig. 2.—Chronic eczema of arm, showing punctate appearance.

parasitics, indicating a possible parasitic origin. It is most likely to occur in fat babies, and rarely persists more than a few months.

2. *True Eczema.*—If one wishes to make a definition of eczema in a narrow sense, it may be said that the characteristic lesion is a vesicle. These lesions may be seen in all stages of evolution, and often may be papulo-vesicular with but little vesiculation. When vesicles form, they rupture and exude a sticky yellowish material which forms crusts. Scratching gives rise to a punctiform appearance which many dermatologists believe is quite characteristic of eczema, and some go so far as to say that the diagnosis of eczema should not be made unless this punctiform appearance is present. (Fig. 1.) Eczema papules and vesicles may appear on a previously healthy skin, or may be engrafted upon a seborrheic dermatitis. Mixed forms are very common. Itching is severe, and a great deal of secondary pathology is caused by scratching and rubbing. The primary damage is a papule, then a vesicle: rub-

bing, scratching, and infection cause infiltration, fissuring, and pustulation—in fact, a great deal of what one sees in any case of eczema is not the primary eczema, but these secondary manifestations. Scaling occurs to a certain extent, but is by no means so prominent as in the previous or in the following group.

The so-called "neurodermite," which occurs often in children of from two to five years of age who have had acute eczema in infancy, is characterized by thickening and lichenification, and is seen particularly in the flexures of the knees and elbows, around the wrists, and

Fig. 3.—Erythrodermia.

on the back of the neck. It is regarded now by most dermatologists as a chronic eczema, with more or less permanent changes produced in the skin by continued mechanical irritation. (Fig. 2.)

3. *Erythrodermia Desquamativa.*—This was first described by Leiner[2] in 1908. Since then it has frequently been discussed in the German literature, but very little in the American. It is characterized by a diffuse inflammatory redness often covering the whole body, accompanied always by desquamation, and usually by seborrheic manifestations. The scales may be large, so that whole flakes of the horny layer of the skin are detached, as in scarlet fever, or they may be fine and branny. The skin is at first not thickened, but after the process has

continued for some time, considerable thickening may be evident. The skin is not dry, but excessive exudation is not present unless rubbing or scratching bring about a good deal of "weeping." This exudation does not tend to form crusts as much as does that of true eczema. The general condition of these infants is almost always poor; indeed, they may be in a state of athrepsia, and diarrhea is very common. There is a general glandular enlargement. At autopsy Leiner found degeneration of the heart muscle, fatty degeneration and infiltration of the liver, and catarrhal changes in the intestinal mucosa. In the skin there was a dilatation of vessels in the papillary region and an increase of leucocytes, with slight inflammation, edema, and parakeratosis of the epidermis. (Figs. 3 and 4.)

I believe that I am describing the same disease to which Moro and Leiner refer, as its clinical picture is unmistakable, and yet, as I have seen it in this country it differs in certain respects from their descrip-

Fig. 4.—Erythrodermia.

tions. They have seen it almost exclusively in breast-fed infants, and believe that the addition of cow's milk to the diet is of specific value in treatment. I have seen only one case in a breast-fed infant, and inasmuch as all the others have been bottle fed, I have not been able to believe that there is any specific virtue in cow's milk therapy. In fact, I have seen 4 patients cured by removal of cow's milk and substitution of a milk-free diet. According to Moro, skin tests with proteins are rarely positive; according to my own experience it is not at all uncommon for them to be positive, especially to egg, but so far I have not seen a case where removal of the food to which a positive test was obtained cured the patient. According to Leiner and Moro, it rarely lasts more than a few weeks: I have seen it last many months. According to all the German authors, it is a disease with a high mortality; I have as yet seen only one patient with this disease die. It is undoubtedly much more common in Germany than here, for although there are in my series approximately 600 infants and young children

with "eczema," I have seen only 13 which fit into the group of "erythrodermia desquamativa." One characteristic which is not mentioned by other writers is blueness of the hands and feet. In all of our cases the hands and feet have been very blue, very cold, and clammy, and this appearance is so striking and so characteristic that I regard it as one of the distinguishing features of the disease. This condition somewhat resembles dermatitis exfoliativa, but is not the same thing. Moro regards it as a greatly intensified seborrheic dermatitis, and believes that it bears but little relation to true eczema or to allergy. Whether this is correct, or whether it represents the eczematous process, probably allergy, in its most severe form modified as to its skin manifestations by various unknown factors, I do not feel at all certain. Its clinical appearance is, however, so distinctive, that whatever its exact place in nosology may be, it warrants inclusion in a separate group. That it represents some profound systemic intoxication, there can be no doubt, and that it is essentially a disorder of the vasomotor system seems probable.

*Summary.*—There are three different elements concerned in the group ordinarily called "infantile eczema": the seborrheic, the erythrodermic, and the true eczematous. In some cases one element may predominate to such an extent, or even be present alone, that definite classification is possible; in the majority the picture is not so clear.

An attempt to place cases of infantile eczema into one or another of these three groups should be made, and, in the course of time, as our knowledge of etiology increases, it will give us a much clearer idea of the whole subject than we have had hitherto.

## The Skin Tests

It has been well known since the original work of Schloss in 1914 and of Blackfan in 1916, that eczematous infants are likely to give positive skin tests to proteins, usually food proteins, and these tests have been widely used in this country in an attempt to determine what was causing the eczema, and to cure it by removing the offending food from the diet. This, however, is by no means always or even often successful. What is a skin test, and what does it mean? In a positive skin test there is a dilatation of the small blood vessels of the skin, giving rise to an area of erythema, and if the vessels are sufficiently dilated, serum exudes and causes a wheal to be formed. Infants under the age of three months are not likely to show positive skin tests, and most infants are more likely to react with erythema alone than with a wheal. In these infants there is something fixed in the skin cells (the reagin), or some change in their biologic properties which causes a vasodilating substance to be formed when specific antigen comes into contact with them. This substance may be activated

or liberated in a number of ways in eczematous infants: by union with the specific antigen, either applied directly to the skin or brought to it through absorption from the digestive tract, or probably likewise by nonspecific antigens, such as other proteins, light, heat, or many other substances applied externally. It also fits in with the facts of eczema that this vasodilating substance may be liberated by mechanical means, such as rubbing or scratching, for many eczematous infants give large reactions to simple scratching before the specific antigen is applied. We are dealing with skins which react to many substances to which a normal skin does not react. The process, infantile eczema, is primarily a capillary dilatation brought about by many different agents acting possibly directly upon the nerve endings of the sympathetics which control capillary dilatation and contraction, or more likely upon the skin cells which then liberate a vasodilating substance. According to the work of Thomas Lewis, the capillary dilatation seen in normal persons when the skin is scratched is brought about by a histamine-like substance freed from the tissue cells by mechanical trauma; in eczema we have this process going on greatly intensified, brought about by many different agents, and with a greatly lowered threshold, for Bloch has shown that the skin of eczematous persons is many times more sensitive than that of normal persons, to almost any sort of stimulus.

The process going on in a positive skin test is the same that occurs in the production of the eczema, although it does not go so far, i.e., vesiculation. However, by the continuous application to the skin, of a food to which an infant is sensitive, it is possible to produce the characteristic lesions of eczema (Moro), and this is also done by Bloch's patch test for external irritants.

The skin tests in infantile eczema often do not help in actually dealing with the patient, but they have done much in giving us what little understanding of the disease we have, and it is desirable to do skin tests on all severe cases.

The cutaneous method of testing is that which has been generally adopted, and while it is not so delicate as the intracutaneous method, it is more practical for clinical use. The method of passive transfer (see page 144) is likewise not practical for ordinary clinical use, but may be of service occasionally if the skin of the patient is so covered with inflammation that direct skin tests are not possible.

The technic used for infants is of some importance. It is desirable to use a scarifier with which the scratches may be made quickly, and which will give scratches of uniform size and depth. I have used needles of various shapes, small knives, and toothpicks, and have not been satisfied with any of them, so I devised a new scarifier. I made the original one from a small leather punch, the later ones are made

by a surgical instrument maker.* The cutting edge of this is in the form of a circle, 90/1000 of an inch in diameter, and sharp on the edges, so that with one quick turning motion a small cut is made in the skin, which on account of its being a circle, is always of the same length, and after a little practice it is possible to make the cuts of uniform depth as well. The skin must be broken, but not deeply enough to draw blood, or, at any rate, much blood. The use of this simple little tool has greatly simplified skin testing in infants and young children, as it is almost painless, and much quicker than any other method of scratching I have yet seen. (Fig. 5.)

Instead of using 1/10 sodium hydrate as the liquid with which to mix the protein powder after it has been applied to the skin, we use physiologic saline solution, as some eczematous infants have such irritable skins that the reactions may be obscured by the irritating effect of the sodium hydrate.

Fig. 5.—Author's scarifier.

The interpretation of the tests needs some experience; for with infants large wheal formation is not the rule, and what one usually gets in a positive test is an area of erythema, large or small, depending upon the technic used and on the sensitivity of the skin. The sensitivity of infants varies greatly: some infants with dermographism (common in eczema) will give large areas of erythema to every test applied; others give only small areas of erythema to one or two tests, and practically no reaction to the mechanical trauma of the scratch. On account of this difference in the reactivity of skins, there can be no definite size standard by which to judge a positive test. If the skin is so sensitive that "positive" tests occur to every protein applied, some of these will usually show whealing, and we take the wheals which occur first, last longest, and are the largest, as the most

*Broadbent & Co., Huntington Avenue, Boston.

important. Sometimes, however, large areas of erythema without wheals develop simultaneously at the site of every test: in these cases it is not possible to draw any conclusions except that the patient has a very sensitive skin. In spite of these difficulties it is in most cases possible to determine the reacting protein, for usually the amount of trauma incidental to the scratch is sufficient to produce only a transitory area of erythema of small size, and a really positive test gives a larger area which lasts longer.

Skin testing in infants is not an entirely accurate procedure, but enough so to be worth while, and to give a fair idea of sensitivity.

*Proteins Used.*—In infancy, if sensitization exists, it is almost always due to foods. It is not necessary to test with a large variety of substances; we have two printed slips, one being a list of proteins for infants under six months, one for those over six months. If special indications exist, we do any other additional tests that may be indicated.

| *Routine Skin Tests* (Under six months) | *Routine Skin Tests* (Over six months) |
|---|---|
| 1. Lactalbumin<br>2. Casein<br>3. Egg white<br>4. Egg yolk<br>5. Barley<br>6. Wheat<br>7. Oat<br>8. Tomato<br>9. Orange<br>10. Wool<br>11. Silk<br>12. Orris<br>13. Cat hair | The same as in the first list, plus corn, carrot, spinach, potato, pea, haddock, beef, chicken, lamb. |

*Results.*—I have had in private and in hospital practice to date 605 cases of eczema in infants and young children, and have done skin tests on 200 of these, all severe cases. These were of all types: some "true eczema," some of the seborrheic type, some of the erythrodermie. Of the 200 cases tested, 125 gave positive reactions, a percentage

TABLE I

POSITIVE SKIN TESTS
(200 Cases Tested)

| | | | | | |
|---|---|---|---|---|---|
| Egg | 89* | Corn | 6 | Carrot | 2 |
| Milk | 37† | Silk | 4 | Tomato | 2 |
| Wheat | 21 | Haddock | 3 | Walnut | 1 |
| Barley | 12 | Orris | 3 | Potato | 1 |
| Oat | 8 | Chicken | 3 | Wool | 1 |
| Beef | 7 | Orange | 3 | Lamb | 1 |
| Spinach | 6 | Pea | 3 | Salmon | 1 |
| Cat hair | 6 | Codfish | 2 | Dog hair | 1 |

*Twenty-eight reactions to egg white alone, 13 to egg yolk alone, 47 reactions to both egg yolk and egg white.

†Six reactions to casein alone, 9 to lactalbumin alone, 22 reactions to both casein and lactalbumin.

of 62.5 per cent. Of these, 89 gave reactions to egg, 37 to milk, 21 to wheat, with a few reactions to various other proteins, as shown in the accompanying table. Fifty gave reactions to one protein alone, and 75 gave multiple reactions.

It is not possible to predict in advance from the appearance of the skin whether tests will be positive or negative, but in general it may be said that those showing the characteristic appearances of "true eczema," i.e., vesiculation and punctate appearance, are the ones most likely to react. I have had, however, positive reactions in pure seborrheic dermatitis and in erythrodermia, and negative ones in "true eczema."

*Skin Tests With Protein-Split Products.*—It is well known that in animals no substances other than proteins will cause the anaphylactic reaction. In allergy in human beings the situation is somewhat different and many physical and chemical agents other than true proteins may bring about an allergic response.

I have seen many patients with eczema, who gave negative tests to milk protein, cured or be improved by the withdrawal of milk from the diet, and from this developed the idea that possibly the eczema might not be due to whole milk protein, but to absorption of partially digested protein—i.e., peptones and possibly polypeptids or amino acids. With this in view the Arlington Chemical Company very kindly prepared for me by artificial digestion egg white peptone, wheat peptone, milk peptone, and casein "aminoids." This last product is biuret-free, contains 0.21 per cent of total nitrogen of which 59 per cent is in the form of amino nitrogen, and consists of a mixture of the end-products of casein digestion.

I have made skin tests on 27 eczematous infants with these substances, in addition to the whole proteins, with the following results:

19 gave positive reactions to whole milk, egg, or wheat protein*
8 gave positive reactions to egg peptone
3 gave positive reactions to milk peptone
3 gave positive reactions to wheat peptone
3 gave positive reactions to casein aminoids

*A higher percentage than in our whole series. In this small series there probably happened by chance to be a sequence of sensitive children.

There were 4 who gave negative tests to the whole protein and positive to the split, 2 to casein aminoids, and 2 to milk peptone. There were 9 who gave positive tests to the whole protein and negative to the split.

It is therefore possible to obtain positive skin tests occasionally with the products of partial protein digestion, and sometimes tests with these products may be positive when tests with the whole protein are negative. I believe that this may be of some importance, particularly

as regards milk. Most bottle-fed infants are taking a very large amount of milk protein in relation to their weights, and also in relation to their digestive capacities. It is not unreasonable to infer that some of this may not be completely digested, and that it is possible for these products of incomplete digestion, when absorbed, to be eczematogenous. We have seen good results follow a milk-free diet when instituted in accordance with positive tests to "casein aminoids" when the test to whole casein was negative. I have not had the opportunity as yet to do tests with these split products on a large enough group of infants to be able to make definite statements, but it is possible, as regards milk especially, that split protein products are of importance.

*Value of Skin Tests.*—It may be concluded as a result of the studies in passive transfer made by many observers in the last few years, that a positive skin test to a protein nearly always means a specific sensitization to that protein. With a young infant who is taking no food except milk, skin tests to other foods than milk tell us little that is going to help in the practical dietetic treatment of the eczema. They do tell us, however, that the individual belongs to the allergic group, and that as he grows older and begins to take other foods, we should avoid those to which he gives positive tests. If the infant is eating foods to which he reacts, we have, of course, definite indications for dietary regulation (see page 154).

## Etiology

There are many etiologic factors concerned in infantile eczema, and it is not easy to evaluate their relative importance. Most of them are secondary or contributory. It is clear that factors which cause eczema in those predisposed have no effect on the majority of infants. We must look for some primary cause which renders the infant susceptible, and places him in the group of those prepared for eczema. His actual eczema may then be brought about by any one of a number of agents.

*Allergy.*—As evidence continues to accumulate, it becomes plain that a large number of eczematous infants are allergic, and the conception of allergy as a fundamental cause goes far in explaining many, but by no means all, of the manifestations of infantile eczema. It has been determined many times that eczematous infants give positive skin tests to proteins much more frequently than do normal infants. Much confusion and apparent contradiction has arisen by finding that many infants give positive tests to foods which they have not eaten, and which could in no way be directly operative in causing the eczema. Allergy may be specific or nonspecific. Specific allergy paves the way for nonspecific allergy, and the assumption that an infant is sensitized

to some specific protein either in utero or possibly in postnatal life through the breast milk, which sensitization not only renders him sensitive to that particular protein, but also places him in the group of allergic persons, so that he may become sensitive to many other proteins or physical or chemical agents as well, explains much in eczema.

There are many facts which support this assumption, and it makes clear many apparent contradictions. Let us consider in more detail the development of sensitivity.

*The Passive Transfer Reaction.*—If a small amount of the serum of a person who is sensitive to some specific antigen, such as egg white, be injected into the skin of a non-sensitive person, the skin in that particular area is rendered specifically sensitive, so that if after a few hours a skin test is done with egg white, at the site of the original injection, a wheal with erythema results. By the combination of three factors; namely, the egg-sensitive serum, the skin cells, and the applied antigen, some substance is formed, or some already formed substance is liberated, from the tissue cells, which is capable of dilating the cutaneous vessels and causing erythema and a wheal. By means of this reaction it has been possible to determine three things of considerable importance in infantile eczema.

1. The fact that the positive reactions to egg, so commonly seen in eczematous infants who have never eaten egg, are specific, and that the serum of these infants possesses the property of transferring egg sensitivity to the skin of normal persons. (Shown by Moro in a large number of young infants.)

2. That the passage of undigested protein through the intestinal epithelium is very common, so much so that it may be considered a normal occurrence. This was first shown by Walzer in 1926[3] with fish protein, and later, in 1928,[4] with egg protein. He injected egg-sensitive serum into the skins of normal persons, and the next morning had them eat raw egg. In a short time itching began to be felt about the site of the previous day's injection, and soon a characteristic wheal developed, showing that the antigen had been absorbed unaltered. Of all the proteins, egg white is the most difficult of digestion, and the most likely to be absorbed in its native state. Fig. 6 shows a reaction following the eating of an egg the morning after the arm had been rendered sensitive by the injection of an egg-sensitive serum from an eczematous infant. Walzer found that this reaction took place in 85.3 per cent of 34 subjects tested, and he states that the absorption of unaltered egg protein may be considered a normal phenomenon. It is likely that other proteins are not absorbed with the same facility as egg.

It is therefore evident that pregnant women are continually absorbing unaltered egg protein, and probably other unaltered proteins

as well, into their general circulations. Ratner has shown experimentally that the placenta is permeable to native proteins, so that unaltered protein reaches the fetal circulation, and he has also many times noted clinically that overindulgence in a certain food during pregnancy may be followed by specific sensitization of the infant to that food. He has noted this so many times and has controlled his observations so carefully, that there can be no question that there is present a cause and effect relationship. I have also noticed this relationship occasionally, and I think there is enough evidence now available, both experimental and clinical, to be able to assume that sensitization of the fetus in utero is not only certainly possible, but probably very common. That it is the primary step in the development of many allergic eczemas in infants seems very likely.

Fig. 6.—Arm showing large reaction after eating egg.

3. That the passage of native protein may occur in breast milk, and that sensitization may be produced in this way. This was first studied by O'Keefe,[5] and later by Shannon,[6] who believed that it was common, and that it accounted for many manifestations of allergy in breast-fed infants. Their ideas caused a good deal of discussion. Some observers confirmed their work, some contradicted it; a detailed critical discussion of these investigations would be out of place here. The last experimental work of which I have knowledge is that of Donnally[7] and of Smyth.[8] Donnally showed definitely by very ingenious use of the passive transfer reaction that the protein of egg eaten by lactating women might be eliminated in their milks in very small but detectable quantities.

Smyth injected egg-sensitive serum into the skins of 36 newly born breast-fed infants, and then fed the mothers large amounts of egg. In no case was there a reaction at the site of injection, not disproving

Donnally's findings that egg was present in the breast milk, but proving that if it were present there was not a sufficient amount to cause a reaction in the baby.

From the experimental point of view the question is not settled, but it would seem from present evidence, that sensitization by means of breast milk is not so important in producing the original specific sensitization in eczematous infants as sensitization in utero. That it may be important secondary to an already existing sensitization, and that it must be taken into account in the practical management of a patient, is indicated by the clinical evidence.

*The Special Rôle of Egg Protein.*—It is becoming increasingly evident, especially in view of the newer investigations, that egg protein plays a very important part in the chain of events which occurs in the development of infantile eczema. In Schloss' series, 53 patients under sixteen months of age were tested: 34 reacted to egg white in spite of the fact that they had never eaten it. In Moro's series (confined to "true eczema") 80 per cent reacted; in our own series 89 out of 200 tested reacted to egg, and of these 50 had never eaten it. Forty-one patients reacted to egg alone. Of the 200 patients there were 125 who reacted to some protein, and of these only 36 did not react to egg.

That the egg reaction indicates specific sensitization and is not due to the fact that there is some quality about egg protein which makes it especially irritating to the skin has been proved by Moro, who not only obtained passive transfer reactions, but also found precipitins for egg white in every infant who gave a positive skin test to it. Of all proteins egg white is the most easily absorbed unchanged through the intestinal epithelium, and it does not need to be ingested in large amounts for some of it to go through into the general circulation. As an illustration of the small amounts that may produce a reaction, the following experiment is of interest. I sensitized an area on my own arm with serum from an eczematous infant who was egg-sensitive. The next day I ate a few cookies containing egg, and a large reaction developed at the sensitized site.

Almost all cases of infantile eczema develop in the early months of life before any egg has been ingested, and most of them are bottle fed (in America, at any rate), so there can be no question of egg in the milk supply. Furthermore, it is not usual in older eczematous children who are eating egg, and who are egg-sensitive, to cure the eczema by removing egg from the diet. If we are to attach great importance to egg in infantile eczema, it must therefore be not as a direct cause, but as an indirect one, and it is probable that primary sensitization to egg in utero (or in some cases to other proteins) is the basis upon which the development of the eczema rests, by producing allergy.

Then allergy may branch out in a number of directions, depending upon the presence or absence of many factors. In some cases primary sensitization to egg protein is followed by secondary sensitization to milk protein, and the eczema is promptly cured when a milk-free diet is substituted. In other cases there may be sensitization to egg alone, and no improvement whatever when a milk-free diet is substituted, indicating that there is a possibility that after egg sensitization some change takes place in the skin that renders it sensitive to *any* protein or conceivably to other substances absorbed from the digestive tract.

We are indebted very largely to Moro for this conception. It fits in well with the facts, and sheds much light on the process going on in the development of many cases of eczema.

It must not be forgotten, also, that allergic conditions are often truly hereditary, transmitted by the germ plasm. In such cases, the general tendency to sensitivity is transmitted, rather than sensitivity to the same protein to which the parent is sensitive. In asthma, the percentage incidence of positive family histories, according to the figures of various observers, is from 40 to 70 per cent. In Rackemann and O'Keefe's large series of eczematous infants and young children, however, there were only 28 per cent with positive family histories of some form of allergy. I believe, likewise, that true hereditary transmission is relatively unimportant in eczema, and while I have seen a good many eczematous infants whose parents have been allergic, it is much more common to find a negative than a positive family history of allergy.

*The Rôle of Trauma.*—The importance of trauma cannot be overestimated. I believe that it is seldom important as a primary cause, but as a secondary cause its significance is paramount. The soil must be prepared by specific sensitization, then it is unduly sensitive to any irritant, internal or external. If the skin of a normal person is rubbed, abraded, scratched, or irritated in any way, it soon shows a tendency, if left alone, to return to normal. The eczematous skin shows this tendency to a lesser degree, and furthermore, it is not left alone. There is continual itching; therefore, there is continual rubbing and scratching, and it is next to impossible, particularly with older infants, who are strong and active, to prevent this. Indeed, some dermatologists believe that the itching is primary, and that there would be no eczema if it were not for rubbing and scratching. I cannot fully subscribe to this, for I have had a few cases where it was possible by means of superlative nursing care to prevent external trauma entirely, and I have seen eczematous lesions develop none the less.

*The Rôle of Infection.*—The rôle of low-grade infection is probably of considerable importance—just how important, it is not easy to determine. There is a sodden, thickened skin, broken, fissured, covered

with débris, and it would be strange indeed if infection did not flourish on such a soil. Sometimes this is of the frankly pustular or furuncular type, and is obvious; again, it may not be so obvious, but I have so many times seen boric ointment or ammoniated mercury ointment do good to a diffuse eczema, even in the absence of pustulation, that it seems likely that bacterial infection may be present without pustulation, and may be doing a good deal to keep the eczematous process active. (Fig. 7.)

Fig. 7.—Infected eczema.

*The Rôle of Fungi.*—In the last ten years fungi have assumed great importance in dermatology, and many hitherto obscure eruptions in adults have been found to be caused by fungus infection, and have been cured by antiparasitic treatment. It is natural that attention should have been directed to infantile eczema as a possible fungus infection, and White and Swartz[9] of Boston, and Cleveland White[10] of Chicago have investigated the problem.

In 1928 White and Swartz isolated a yeast-like organism (cryptococcus) from a number of cases, and were able to improve or cure these by antiparasitic treatment. They did not reproduce the disease by inoculation. They say that this organism never gives rise to moist or vesicular lesions (hence do not resemble "true eczema"), that the lesions are of a light *café au lait* color, are deeply infiltrated in the later stages, and that their progress is very slow.

Cleveland White secured cryptococcus cultures from 77 per cent of a series of cases of infantile eczema, and was able to reproduce the disease a number of times on healthy portions of the skin by inoculation from the original lesions. He claims only that yeast fungi may be the cause of some cases of infantile eczema, and is not certain whether their principal rôle is saprophytic or parasitic. "It is not surprising that yeast species should be isolated from extensive superficial dermatoses like infantile eczema; their pathogenic rôle remains to be determined."

The finding of fungi in eczema lesions means comparatively little; the prompt disappearance of these lesions under antiparasitic treatment means a good deal. I have had a number of cases of the seborrheic type, with rather sharply defined scaling moderately infiltrated lesions, where cure with antiparasitic treatment has been so much more rapid than it possibly could have been in any ordinary case of eczema, that it seemed to me I must have been dealing with a parasitic infection. I have seen a number of patients with infantile eczema, the mothers of whom had definite epidermophytosis of the hands, beginning after the child's eczema began; whether any significance can be attached to these cases or whether they were merely coincidences, I am not prepared to say. I have the impression that there is some relation between fungus infection and allergy, and that fungus infection is more common in allergic than in normal persons, sometimes as a very late manifestation.

In order to determine accurately the rôle of fungi, it is necessary to isolate the fungi in question from the lesions, reproduce the lesions by inoculation on healthy skin, and cure them by antiparasitic treatment. This is beyond the range of all pediatricians, and of most dermatologists, for mycology is a science in itself, and the processes involved are too complicated.

Not being a dermatologist it is perhaps presumptuous for me to express an opinion concerning a subject over which skilled dermatologists are in disagreement, but if I may be forgiven for doing so, it seems to me that there is enough evidence to indicate that fungus infection may play a certain rôle in some of the cases called "infantile eczema," possibly a primary rôle, and that if a fungus is operative,

the eczema is most likely to be manifested by rather dry, oval, or rounded lesions of various sizes, scaling, not of as deep a color as the ordinary eczema, not vesicular, and rather sharply circumscribed in outline; that these cases are, however, of small importance and of infrequent occurrence in comparison with the great number of allergic cases, and that fungus infection plays a minor rôle in the group "infantile eczema."

*External Irritants.*—At the present time the majority of dermatologists believe that in most cases of eczema in adults external irritants are of vastly more importance than internal, and that foods play an unimportant part. Eczematogenous substances are innumerable, indeed eczema may be caused by almost any substance with which the person may come into contact. Their eczematogenous quality is determined by specific sensitivity of the person, and the skin of the sensitized person reacts to external substances to which the skin of normal persons does not react. Most cases of eczema in the adult, according to this conception, are exactly analogous to what has hitherto been called "dermatitis venenata"—thus "poison ivy" is an eczema. Bloch has devised the so-called "patch test," in the performance of which various suspected irritants are applied in small quantity to the unbroken skin and held in place by adhesive tape for twenty-four hours. A positive reaction consists of erythema and vesiculation at the site of inoculation. The application of this test has been of much value in dermatologic practice, and many times determines the etiology of obscure cases of eczema.

The conditions are, however, somewhat different for infants, and it is our opinion that sensitization to external substances is of relatively small importance in infantile eczema. Mechanical irritation from scratching and rubbing plays an important part, as we have already said; changes in temperature, exposure to the wind, application of strong soap: all these aggravate an already existing eczema; but it is decidedly uncommon to find an infant who has developed eczema from contact with any external chemical agent to which he is specifically sensitive. The infant comes into contact with relatively few external irritants, and most of the evidence we have indicates that the development of infantile eczema depends more upon internal than external factors. I have seen a very severe case of eczema in a young child from sensitization to dog hair, which was promptly cured when the dog was disposed of, and I have seen several cases with sensitization to silk and wool, but these are the only ones I have seen where it was clear that the eczema owed its origin to external specific sensitization.

*Teething.*—There is a widespread belief among mothers that eczema may be caused by difficult dentition. This is certainly not true,

but I have seen so many cases of already existing eczema become worse while a tooth was being cut, particularly if there was any difficulty with it, that I am inclined to the belief that there is some relation between difficult dentition and the exacerbation of an eczema. It may be that this relationship exists through the sympathetic nervous system. It is probable that abnormality in the sensibility of the capillaries and small arterioles of the skin is one of the basic facts of infantile eczema. These are controlled by the sympathetic nervous system, and it is conceivable that any influences which might bring about an increased irritability of this, might cause an exacerbation of the eczema.

*Overfeeding.*—It is a clinical fact beyond dispute that many eczematous infants, particularly those fed upon the breast, are fat and overfed, and that the eczema tends to improve if the food intake is reduced. It is also a fact of common observance that if an eczematous infant becomes ill with some intercurrent infection and eats very little for a few days, his eczema at once improves or disappears entirely, only to reappear as soon as he begins to eat again. This is explained either by the fact that during partial starvation he is ingesting in minimal quantities some particular protein (milk usually), to which he may be specifically sensitive, or that a large amount of food in general influences the eczematous process unfavorably. This may be operative in a number of ways:

1. By influencing the nutrition of the skin. It cannot be said that overfeeding in general is often the primary cause of eczema, for most eczematous infants are not overfed. It is true, however, that the type of eruption, and often its intensity, may depend upon the nutrition of the infant, and upon the chemical constitution of the skin tissue—whether high or low in fat, water, salts, of high or low hydrogen ionization, and so on. Fat infants are likely to have a moist type of eczema, with a good deal of crusting; in poorly nourished infants the eruption is likely to be dryer, and with more tendency to scaling.

There is, however, very little definite information available as to exactly what conditions of metabolism increase or diminish skin irritability.

2. By the direct influence of toxic products from decomposition of or incomplete digestion of food. Special attention has been directed to the fat, and it is true that in some cases reduction or omission of this food element is of benefit. This may be due simply to changes in the nutrition of the skin from having reduced the caloric intake, or possibly to some deleterious effect of fatty acids, or in allowing less undigested protein to be absorbed by rendering casein digestion easier, for if in the stomach the casein curd is intimately amalgamated with fat, its digestion becomes more difficult.

There is an opinion among mothers and some doctors that reduction in the sugar is of benefit in eczema. I have seen very little evidence to support this, or that one sugar is different from another in its eczematogenous properties.

It is probable that protein is the most important of all the food elements. I have seen how common the absorption of undigested protein is even in normal persons, and that the amount absorbed is directly proportional to the amount ingested cannot be doubted. It is therefore desirable not to overfeed with protein, and to offer it in an easily digestible form. It is also possible that not only protein, but protein decomposition products may be of some importance, and it is of interest to note that histamine, which is *the* capillary dilator par excellence, and which is assuming more and more importance in allergic conditions, may be formed from almost any protein. There is evidence to show, however, that it loses some of its vasodilating properties when absorbed through the digestive tract.

As regards the salts, little definite information is available. Finkelstein for a number of years recommended a diet very low in sodium chloride, and it was found to be of some benefit, probably largely because of water loss from the tissues.

As a summary, it may be said that while it may be true that various individual constituents of the diet influence the eczematous process one way or the other, that very little is definitely known about these relationships, that for practical purposes, a well-balanced, not too liberal, normal type of diet is indicated in most cases, and that aside from the question of specific idiosynerasy, not a great deal will be gained by focussing on one element of the diet. Stuart[11] once said, "We may conclude that the etiologic agent producing eczema is least effective under conditions of minimal skin, and minimal gastrointestinal irritation."

## SECTION II

### Practical Treatment

The foregoing has been largely an attempt to show the nature of the disease, and to trace its development as clearly as possible. Necessarily much of this has been theoretical and speculative. There are, however, enough concrete facts upon which to base a reasonably intelligent and moderately effective treatment.

Adequate knowledge of a disease presupposes three things:

1. We must be able to separate the disease clearly from other diseases.

2. We must know its etiology.

3. We must have at hand a therapy which is effective in the majority of cases.

For infantile eczema, not one of these postulates is entirely fulfilled, and yet it is not impossible by appropriate treatment to secure excellent results in some, and fair results in many cases.

*The History.*—There are certain points in the history which are of importance in the practical management of any case.

1. Is there any history of allergy in the family?
2. Did the eczema begin coincidently with any change in diet, such as the beginning of bottle feeding?
3. If the baby is breast fed, what are the mother's dietary habits?
4. Has there been any preparation used for local treatment which was found to be of special value?
5. How many physicians have already treated the patient, and what was their treatment, both local and dietetic?

*Hospitalization.*—I used to believe that it was not possible to secure good results except in a hospital, but in the last few years I have somewhat changed my viewpoint. For the most severe cases, those patients covered with crusts and infection, hospitalization is desirable, provided the infant can be isolated from other infants, and provided the nurses understand the care of infantile eczema. There are few mothers who can deal with this type of case, and they are usually so worn out by the sleepless, irritable child that some change in management is imperative, for the sake of the mother as well as for that of the child. The trouble with hospitalization is that eczematous infants are very prone to infection, especially respiratory infection, and an eczematous infant put into a ward with other infants is very likely to develop otitis media, bronchitis, or bronchopneumonia, no matter what precautions are used. If circumstances make it possible to have a private room, hospitalization will do a great deal toward relieving a distressing home situation, and the baby can usually be sent home in two or three weeks with the eczema under such control that sleep and a more satisfactory existence are possible for the mother. The majority of eczematous infants, however, must be taken care of by the mother at home, and with the not too severe type of case, this does very well.

*General Management.*—When one sees a severe case for the first time it has usually been of some months' duration. During this period several doctors have usually been consulted, innumerable salves and lotions have been used, the mother is discouraged, and the baby is often no better. One reason for this is that radical measures have not been taken: the baby has not been looked upon as a sick infant; he has been dressed, taken about, restrained very little; local applications have been applied improperly and too infrequently, and the doctor has not seen him often. An infant with severe eczema should be looked upon as a sick child, and should be put to bed and kept there until he is better; the doctor should see him often, and should pay as much attention to

the whole situation as he would to one which is more dangerous to life.

The matter of clothing is of considerable importance. In applying salves our usual instructions to mothers are "put the salve on often enough so that there will always be some on the skin." It is therefore not desirable to dress the infant in the usual number of clothes; if the eczema covers the trunk, he should wear merely diapers and a soft cotton nightgown. No wool should come into contact with any eczematous infant at any time. Occasionally, it may be desirable to keep the baby naked. If so, he is put into a "light bed," an ordinary crib with a canopy over it, blankets over the sides, and electric lights in it to keep the temperature at 80° F. This apparatus necessitates a good deal of attention, and in spite of the utmost care it is not easy to prevent chilling, so except when the body is covered with oozing and infection, we rarely use it.

*Prevention of Rubbing and Scratching.*—With older infants and children it is not possible to prevent rubbing and scratching entirely, and it is difficult enough even with young infants. I have tried many methods, some complicated, some simple, and have come to the conclusion that tying the arms and legs to the sides of the crib is the best method. Young infants can be kept tied down in this way most of the time, and soon become so used to it that they are much quieter and more comfortable than if they were not tied down. For milder cases, stiff cotton covered cardboard cuffs over the elbows are fairly satisfactory, and I much prefer them to aluminum mittens. The nails should be kept short, and the fingers clean in order to diminish the chance of infection by inoculation from scratching.

*The Use of Water.*—Washing with water has usually been forbidden for eczematous infants. I think, however, that one must not be too strict about this. Water is not desirable for acutely inflamed areas, but there can be no objection to using it on the buttocks and genitalia or on any part of the body that is not covered with eczema, provided it is found not to cause irritation or increased itching. There is a curious disease well known to dermatologists called "bath pruritus," in which there is excruciating itching and tingling of the skin after bathing. Those suffering from this condition usually have dermographism and sometimes evanescent urticaria, and it is probable that it is allied to the eczematous group. I think that some eczematous infants may have this condition to a certain degree, but I think also that there can be no objection to the use of water on normal parts of the skin, if after trial it has been found to do no harm.

*Regulation of the Diet.*—

a. With Positive Skin Tests: There is no one dietary measure that is uniformly successful; each case must be individualized, and differ-

ent plans used according to indications. If skin tests to foods are positive, the corresponding foods should be omitted from the diet, *provided there are not too many of them.* In the early days of skin testing, a great deal of harm was done by removing from the diet every food to which a multisensitized child gave a positive test, with deleterious results to the nutrition of the child, and rarely any good to the eczema. When reactions are positive to a large number of foods, it is likely that there is sensitization to almost any food protein. In such cases if treatment were carried out strictly on the basis of sensitization, it would not be possible to feed the child an adequate diet. This situation, however, does not often arise, and it is not very troublesome to remove from the diet the few foods to which a child may be sensitive. It is not difficult to make up a diet free from egg, wheat, or milk, the three foods which account for most cases of food sensitivity in infancy and childhood.

The results of dietary regulation in accordance with the food tests are sometimes brilliant, sometimes very disappointing. If there is very definite sensitization to one or two foods as indicated by positive tests, and particularly a clinical history of sensitivity to these foods, and there are no other positive tests, indicating the absence of general sensitization, withdrawal of the offending foods may be followed by very prompt improvement or even cure of the eczema, but in many cases the improvement is more gradual, and for this reason it is difficult to judge the value of dietary regulation. If there is a sensitivity to milk in bottle-fed babies, and this is withdrawn, results are almost uniformly good. Withdrawal of eggs is not likely to be so satisfactory, and there are many egg-sensitive children of from two to five years of age, who still have eczema in spite of the fact that they have not eaten egg for months or years.

In short, for older children on a mixed diet, too much must not be expected of the withdrawal of apparently offending foods, and a considerable amount of common sense must be used in connection with the procedure.

b. With Negative Tests: It is well known that an infant may be sensitive to a food and still give negative skin tests. This is particularly true of infants under the age of four months. Here milk comes especially into question. Because I have seen a number of patients with eczema who gave negative tests to milk protein, cured by a milk-free diet, I usually plan to give a milk-free diet a trial for two weeks in all very severe cases, in spite of negative skin tests. For milder cases, with negative tests to milk, I do not like to make the somewhat radical change to milk-free diet, and use as routine foods either evaporated milk or Similac. We use these foods because they are both easily digestible, particularly as regards their protein content, in ac-

cordance with the principles previously expressed. We do not attempt to underfeed the average patient, but supply the caloric needs in the same way that one would for any infant. If the baby is very fat and obviously overfed, we reduce the caloric intake by cutting down the amount of fat.

*The Specific Effect of Cow's Milk.—*

a. Milk-Free Diets: As we have already seen, it is reasonable and in accord with what evidence we have, to look upon most cases of infantile eczema as of internal origin, and furthermore that they arise in some way from the effects of food. Therefore, inasmuch as cow's milk is the only food that most infants are taking when they develop eczema, it follows that the question of this food in its relation to the disease is a most important one. In our series, 37 of 200 patients tested gave positive skin reactions to the proteins of cow's milk. Six of these reacted to casein alone, 9 to lactalbumin alone, and 22 to both casein and lactalbumin. Of those who gave positive reactions to milk, 19 also gave reactions to egg, although most of these infants had never eaten it. The importance of cow's milk in causing eczema is, however, considerably greater than is indicated by the number of positive reactions, for all students of allergy agree that it is not infrequent for sensitization to an antigen to exist, especially an ingested antigen, and for skin tests to this antigen to be negative. Schloss in his earlier work found precipitins for milk in the blood serum of many infants who gave negative skin tests to milk, and Moro more recently has obtained both positive precipitin and passive transfer tests under the same conditions. Rowe disregards negative skin tests to foods to such an extent that he has devised an ingenious series of elimination diets, first omitting one food, then another, to arrive at the one which is causing symptoms by a process of trial and error. It is also well known that young infants are the ones most likely to give negative tests. So it may be concluded with a reasonable degree of certainty that cow's milk is more important as a cause, or at any rate as a contributing factor, in infantile eczema, than is indicated by the number of positive skin tests. Furthermore, it is evident that no infant who is severely sensitized to milk (as in cases of true milk idiosynerasy) is likely to have eczema, for he is immediately made so violently ill by the ingestion of even very small quantities of milk that the unsuitability of cow's milk as a diet for him is at once quite evident, and he never ingests enough of it to give him eczema.

The earlier workers on eczema (Blackfan, 1916 and Schloss, 1920) recognized the significance of cow's milk, and both devised milk-free diets upon which the patients with eczema improved remarkably in a

short period of time. The diets, however, caused severe digestive disturbances, and therefore had to be discontinued. In Germany, likewise, various milk-free diets have been devised, with which very good results have been reported. None of these diets have been available for general use, and all have been rather difficult of digestion.

The importance of cow's milk in infantile eczema seemed great enough to me to warrant the attempt to devise a milk-free food which would be digestible, capable of maintaining nutrition, and which could be manufactured in large enough quantities so that enough eczematous infants could be fed upon it to determine more comprehensively the rôle of cow's milk as an eczematogenous factor. With this in view, Stuart and I devised Sobee, a food made of soy bean flour, olive oil, purified cornstarch, and various salts. This has been described in detail elsewhere.[12] Soy bean flour was chosen as the source of protein because it contains the necessary amino acids for growth, is easily available, and not expensive; olive oil as the fat because it is more easily digestible than butter fat and because we wished to get away as far as possible from cow's milk, and purified cornstarch as the carbohydrate because it is practically protein-free, and by its colloidal properties when cooked with water, aids in the proper preparation of the food. No sugar was added, because we felt that it was best to permit the individual physician to use whatever amount or kind of sugar he desired, according to the indications. This food contains vitamin B probably in adequate amounts, but its content of the other important vitamins (A, C, and D) is low, and care must be taken to add orange juice and cod liver oil or haliver oil. The product is a light brown flour of not unpleasant taste, and contains:

| | |
|---|---|
| Fat | 22.5% |
| Protein | 33.2% |
| Carbohydrate | 32.6% |
| Salts | 8.5% |
| Moisture | 3.2% |

1 ounce = 134 calories
6 level tablespoons = 1 ounce

The standard dilution is 1 ounce (6 level tablespoons) to 7 ounces of water. When mixed in this proportion the composition is as follows:

| | |
|---|---|
| Fat | 2.8% |
| Protein | 4.2% |
| Carbohydrate | 4.1% |
| Salts | 1.0% |

1 fluid ounce = 17 calories

In using it I have ordinarily started with about three-fourths strength, i.e., 5 level tablespoonfuls to 8 ounces of water, and increased as tolerance became established.

Such a food is a radical change from milk feeding. The questions that arise before considering whether or not it does any good to eczema, are:

1. Will babies take it?
2. Will they digest it?
3. Will they thrive upon it?

Many babies take it immediately, and there is no difficulty whatever in making the change from milk feeding. The younger the baby, the more likely this is. Some take it poorly for a few feedings, and then take it well. A few, according to the mothers, will not take it at all. This last statement must, however, be somewhat discounted, as most mothers become too easily discouraged when trying to get an infant to take a new food, and it is significant that we have had no hospital patient who refused it. As a general thing it may be said that there is no great difficulty involved in getting most infants to like it, but that a few, older infants especially, may rebel.

I have had some cases in which it caused diarrhea, in some sore buttocks, and in some vomiting. These are not common, particularly if it is started rather cautiously. The stools with Sobee feeding are large, and may be constipated, or sometimes rather looser than with cow's milk feeding, and somewhat more frequent in number. This is not abnormal, and if the buttocks are not sore, and there is no actual diarrhea, the food need not be discontinued.

It may be said definitely that babies thrive upon this food as well as they do when taking milk (provided orange juice and cod liver oil are given). We have fed a number of babies on it for over six months, and they have made good gains in weight and have had excellent tissue turgor. I was recently informed by a visiting physician that she had kept one baby on it for over two years.

I have fed about 80 eczematous infants on this food, and have used it according to the following indications:

1. To all cases with positive skin tests to milk.
2. To a good many severe cases with negative milk tests.
3. To practically no mild cases.

The results are variable. We have had some truly remarkable results in some patients, where in a few days a severe eczema has almost entirely disappeared, and has been kept in this condition as long as Sobee feeding was continued. In other instances improvement is more gradual, and in some there is no improvement, for all cases of eczema are by no means due to milk. If the eczema is due to milk, it will be cured with Sobee feeding.

If no improvement takes place in two weeks, we discontinue Sobee. In about half the cases where it has been used it has been very success-

ful, so that it may be considered, after several years' use, as a very definite help in the handling of severe infantile eczema.

It is no more a cure for all cases of eczema than digitalis is a cure for all cases of heart disease; too much must not be expected of it, and it must be remembered that there is no such thing as a standard dietary regimen that can be always successfully applied.

I think that most of the benefit of Sobee is due to the omitting of milk protein, and the substituting of another protein to which the infant could not have previously been sensitized. It may well be, however, that soy bean protein is more digestible than milk protein, and that the simple question of digestibility may play a considerable part. There may also be other factors of which we know nothing, for the food is radically different from milk in almost all respects.

b. Heated Milks: It is known that allergic persons can sometimes take cooked food without symptoms when raw food causes symptoms. This has been assumed to be due to some change in the protein caused by heat, although the nature of this change is very obscure.

Variot, in 1911, began to write about superheated milk in the treatment of infantile eczema, and since then has published several reports.[13] He used milk heated to 108° C. and homogenized,* and claims excellent results. Kerley, in 1926,[14] advocated prolonged boiling of milk for six hours, and in 1931 the S. M. A. Corporation introduced their "hypoallergic" milk, treated in somewhat the same way.

Comparatively little work has been done to show exactly what change is produced in milk proteins by heat. Besredka,[15] working with guinea pigs sensitized to whole milk, found its antigenic power was not changed when heated to 120° C. for fifteen minutes, that when heated above 120° C. it lost some of its toxicity, and that when heated to 130° C. it was only slightly toxic. Cutler[16] found that in evaporated milk, which is heated to 240° F. (116° C.) for twenty minutes, there was no change in the antigenic properties of the casein, but that the coagulable proteins lost a certain amount of their antigenic properties. As far as chemical changes are concerned, it is not known what changes take place, or indeed if there are any, other than coagulation of the coagulable proteins.

It would seem as though in clinical practice the amount of benefit to be obtained by the use of superheated milk depends upon the degree of sensitivity existing, and whether the sensitivity is to lactalbumin or to casein. I have had too little experience with heated milks to be able at this time to express any very definite opinion as to their value in infantile eczema, and feel that the subject warrants a more thorough investigation.

*Desensitization.*—Specific desensitization; i.e., the parenteral or enteral administration of very small amounts of the offending food, has

*Nothing more than evaported milk.

not been found very practical or of great benefit in infantile eczema, and for this reason I have rarely used it. Desensitization takes a long time, and requires frequent and many treatments. There is considerable danger of producing generalized reactions, and often the eczema grows worse under this treatment. Infants with food sensitivity almost always, as they grow older, "outgrow" it, and acquire tolerance, so that unless the sensitivity is of very severe degree, as in some cases of milk idiosynerasy where a violent general reaction follows the ingestion of even a few drops of milk, attempts at desensitization are not likely to be worth while, and it is usually better to avoid the offending food, until tolerance is established.

Nonspecific desensitization is an attempt to do away with allergy in general, and for this purpose various methods have been used, such as the injection of milk, typhoid vaccine, peptone, and various other nonspecific proteins. It is quite possible that, working along this line, some method will be found by which an allergic person can be rendered nonallergic, and when it is found, a large part of the difficulties of infantile eczema will have been solved. At the present time, however, the results of nonspecific therapy seem altogether too uncertain to warrant its use in practice.

*Breast-Fed Infants.*—I have seen comparatively few breast-fed infants with severe eczema, and it has been my experience that the commonest course of events is for the eczema to appear shortly after cow's milk feeding has been started. The disease in the breast-fed infant may, however, be fully as severe as in the bottle fed, and it is always somewhat perplexing to decide in what way to manage the diet. Almost all breast-fed infants with eczema are vigorous and well nourished, often overnourished, and if breast feeding is to be continued it is always desirable to reduce the amount of food by shortening each nursing period, and by giving water either before or after feeding. In mild cases this often brings about marked improvement.

With severe cases the question of allergic sensitization through the breast milk arises. This has been discussed already in a previous section, and I shall merely say here that I believe from clinical observation that sometimes such sensitization does take place through breast milk, from foods that the mother is eating, and that this aspect of the situation should be taken into account in the practical management of breast-fed infants with eczema. If skin tests are positive to one or two foods only, these may be omitted from the mother's diet; if tests are positive to many foods, which is often the case, I believe it is much better to wean the baby and to regulate the artificial feeding in accordance with the principles already discussed.

*Feeding in Erythrodermia Desquamativa.*—Moro believes that this condition is dietetic in origin, and that it is due to lack of a specific fac

tor, which he calls "vitamin H," plus a too abundant supply of fat. He bases this belief on the fact that somewhat similar skin lesions are caused in rats which are deprived of this factor and upon the high content of fat in human milk. He has not shown, however, that the vitamin bears any relation to the disease as it actually occurs in infants. If this theory were correct, it should be a comparatively simple matter to cure the disease by a diet high in the vitamin (contained in yeast, liver, and carrots) and low in fat, which can by no means be done, and there is no definite proof that lack of any vitamin is a cause of the disease. Schiff[17] investigated this quite thoroughly in 1926, and said: "Through no form of vitamin therapy is it possible to do any good whatsoever to an erythrodermic child." I have seen no particular form of diet upon which erythrodermia develops, or one upon which it can be cured. I have seen some patients who were allergic, some who were not, and I am not convinced that allergy plays no part in the development of this disease. I have seen four patients cured by a milk-free diet, and yet I do not believe that milk is generally the cause of the disease; I have seen one patient cured by weaning to a diet of cow's milk, and I have seen others who could not be cured by any dietary regimen whatsoever.

Most infants with erythrodermia are in a poor state of nutrition, some indeed in a condition of athrepsia, and I believe that until more certain evidence is available concerning some specific dietary factor, the most important part of the treatment is to improve the nutrition, in accordance with the general principles governing the feeding of poorly nourished infants, by any methods of feeding that may seem desirable. I am at present entirely ignorant of any special diet which can be depended upon to benefit these patients, and am trying various types in the hope of arriving at some combination that may be of service.

### Local Treatment

*General Principles.*—If one assumes that infantile eczema is brought about by internal causes, it is futile to hope for a cure by any methods of local treatment. While this is true as regards the primary eczema, it must be remembered that much of the pathologic condition of the skin is secondary to the original eczematous process, and that much may be done for this by proper local treatment. This is of paramount importance, so much so that it is indeed about all we can do for many patients, in the present state of our knowledge. No local treatment, however, can transform an allergic infant into a nonallergic one.

Innumerable preparations have been used and every one who has dealt much with the disease has worked out for himself methods which he has learned to use with success. It is not a large number of salves

and lotions that spells success, but the proper use of a few. There are certain principles which it is well to remember:

1. That the eczema may be in different stages or states on different parts of the body, and lesions on one part may require entirely different treatment from coexisting lesions on another part.

2. That ointments, if the eczema is at all infiltrated, should be rubbed in gently but thoroughly, and not merely spread on.

3. That all preparations, whether ointments or lotions, should be applied frequently enough to keep some on the skin, no matter how frequently the child rubs it off.

4. That it is desirable to teach the mother as much as possible the indications for using the various salves and washes, so that she may shift about from one to the other as the particular state of the skin at any given time demands.

*The Scalp.*—There are few cases in which the scalp is not involved; with either a mild seborrhea or the most extensive crusting and oozing. Scalps are, as a rule, not very hard to deal with, and it is usually possible to control the process without much trouble. I have found the following method of treatment very satisfactory.

Boric ointment (U.S.P. No. 9)* is rubbed and smeared *very thickly* over the scalp in the morning. Several cheap cotton caps are obtained and one is put on as soon as the ointment has been applied, and is left on until the next morning, when more ointment is applied without trying to remove what is left of the previous day's application. A fresh cap is then put on, and the process repeated for five days. On the sixth day the scalp is shampooed with Ivory or Castile soap and water. In many cases one course of treatment is sufficient to cure the process on the scalp. If it does not, after a day or two another course of treatment is given, or as many more as may be necessary.

*The Face.*—The face is the commonest site for infantile eczema, because it has a very rich blood supply with very easily dilatable arterioles and capillaries, and because it is continually exposed. It is also one of the most difficult locations to treat because it cannot be adequately protected, because it is difficult to keep ointment on it, and because it is not possible to prevent rubbing entirely, no matter what methods of restraint are used. I have never found masks satisfactory, and no longer use them.

In the very worst cases the whole face may be one mass of scabs, scales, and crusts, continually oozing and crusting again so that practically no normal skin can be seen. All of this secondary detritus must be removed before any progress can be made. First, as many crusts and scabs as possible are removed by swabbing with olive oil or liquid

*No. 9 is made without wax, and is much to be preferred to the newer No. 10 with wax, as it does not leave so much residue.

petrolatum and gauze. Then boric ointment is applied very thickly, and it must be reapplied frequently, as often as it is rubbed off, so that the face is at all times covered. Once each day all the ointment and softened detritus are gently removed with gauze. After a few days of this there is left a very red, acutely inflamed surface, usually with a good many papules and vesicles, with or without oozing. If there is very much oozing, no more salve should be used at this stage, as salves do not stick well to an oozing surface. To dry oozing we have found nothing so good as the following prescription, originally recommended by Schlotz:

| | |
|---|---|
| Goulard's Extract* | |
| Burow's Solution† | āā ℥ ss |
| Water | ad ℥ vi |

*Liquor of lead subacetate U.S.P.
†Saturated solution of aluminum acetate.

This is sopped on frequently until the oozing is controlled, usually in about two days. If the skin is still very acutely inflamed, the following wash used for two days is of value, before applying tar:

| | |
|---|---|
| Resorcin | |
| Boric Acid | āā ʒ i |
| Zinc Oxide | ℥ ss |
| Water | ℥ vi |

If the skin is not too acutely inflamed, tar is applied at once.

*Crude Coal Tar.*—The use of crude coal tar in dermatology originated in France and was introduced into this country by E. Lawrence Oliver and Charles J. White at the Massachusetts General Hospital about twenty years ago. It is the most efficient agent we have for the local treatment of infantile eczema.

After the preliminary treatment already described has been carried out, the following paste is applied as often as is necessary to keep the skin covered. (Tar Ointment No. 1.)

| | |
|---|---|
| Crude Coal Tar | ʒ ii* |
| Zinc Oxide | ʒ iv |
| Starch | ʒ viii |
| Vaseline | ℥ iv |

*This paste should be prepared by first mixing the tar with the zinc oxide, then the starch with the vaseline, then the two mixtures are combined.

This formula represents the usual strength employed, and the skins of most infants will stand it, but if it causes irritation, as it may occasionally, half the amount of tar is used. Tar should never be used when there is pustulation present.

Sometimes when the eczema is considerably thickened and occurs in the form of circumscribed patches, we use tar alone painted on with a cotton swab, full strength. This soon dries, and forms a protective coat-

ing which adheres better than the paste. This is indeed strong treatment, but is often very efficient. Tar in any form is dirty, and it is therefore desirable to discontinue it as soon as possible. After it has been used for a week or two, and the skin has become less red, smoother, and the tendency to oozing is fully controlled, we shift either to the compound resorcin ointment of the National Formulary (1), or to 5 per cent lenigallol in zinc oxide ointment (2).

| | | |
|---|---|---|
| (1) | Resorcinol | ℥ iss |
| | Bismuth Subnitrate | ℥ iss |
| | Zinc Oxide | ℥ iss |
| | Oil of Cade | ℥ iiss |
| | Petrolatum | |
| | Hydrous Wool Fat | |
| | Paraffin, of each to make | ℥ iii |
| (2) | 5% Lenigallol (pyrogallic triacetate) in zinc oxide ointment | ℥ ii |

If these do well, we continue them indefinitely; if not, we go back to tar paste again. If the eczema when first seen shows little tendency to ooze and crust, we begin at once with tar paste without any preliminary treatment. If the cheeks are merely too red and are fairly smooth, with practically no thickening, it is better not to use tar at all, but to begin with either resorcin or lenigallol ointment.

It is usually possible to accomplish the following with a bad face. The oozing will have stopped, so that there is no more crusting, a good deal of the infiltration and tendency to papulation and vesiculation will have disappeared, and the itching is largely controlled. The cheeks are, however, still abnormally red, infiltrated and scaly to a certain degree, and some days the skin condition may look practically cured; other days it may flare up temporarily, but never becomes as bad as it was before. It is very difficult after this stage has been reached, to bring about an entirely normal condition of the skin, and indeed it must be realized that often this is impossible, and that much of the time all that we can do is to keep the process well under control. After a while, it gradually clears up, probably more because we are able to prevent its becoming worse than by any direct "cure" we can make upon it. Lenigallol is a mild, slowly acting astringent, and does very well in combination with zinc oxide in accomplishing the purpose we desire. Compound resorcin ointment is a very sticky, thick preparation with excellent protective power, and is also astringent and healing to a certain extent; I have found that either one of these preparations do better at this stage than any others I have used. If a flare-up occurs, we go back to tar paste for a while, but if the skin becomes much wrinkled and drawn, it is a sign that it is being overtreated with tar, and a simple protective salve, such as plain lanolin, is used for a few days.

*The Body.*—On the body, the eczematous condition may be generalized or patchy. In one form (the seborrheic) there may be few or many large or small lesions, which are slightly infiltrated, usually dry, scaling, and pinkish red in color. If the body is well covered with these, I have used with considerable success a somewhat different tar salve. (Tar Ointment No. 2.)

| | |
|---|---|
| Crude Coal Tar | 5% |
| Yellow Wax | 15% |
| Petrolatum | 40% |
| Hydrous Lanolin | 40% |

This is a smoother ointment than the tar paste, and is much better where it is desired to treat large dry surfaces. It should be well rubbed in, and it is not necessary to use it very thickly.

If the scaly patches are small and few in number, it is better to use a paint than a salve, as it is not easy to keep a salve on a small patch on the body long enough to do much good. For such patches I use

| | |
|---|---|
| Crude Coal Tar | ℥ ii |
| Acetone | ℥ ii |
| Flexible Collodion | ℥ i |

This is applied with a camel's hair brush once a day.

If the body is covered diffusely with small papules and papulovesicles (so-called diffuse acute papular of vesicular eczema), starch baths are used in combination with tar ointment No. 2. A solution of cornstarch is made in about the same strength that one would use for starching linen. This is sopped on all over the body in the morning, allowed to dry, and the ointment applied at night. Sometimes simple whitewash is used instead of the starch bath.

| | |
|---|---|
| Zinc Oxide | ℥ ss |
| Limewater | ℥ viii |

If the body is diffusely red all over, with many large or small scales (erythrodermia), none of these methods should be used.

*The Arms and Legs.*—The arms and legs are common sites for eczema. On these sites the process is usually infiltrated and only moderately oozy. Tar ointment No. 1 is applied twice a day, and is kept on by cotton stockings or loose bandages; small places may be painted once a day with the undiluted crude tar.

*The Ears.*—There are often small oozy cracks behind the ears. If they are not too oozy, they are painted with crude tar; if very oozy I use the Goulard's Extract and Burow's solution until the excessive oozing has been controlled, and then apply the tar.

*Chronic Eczema in Older Children* (two to ten years).—This usually manifests itself by reddened, infiltrated, sometimes lichenified areas of diffuse character, behind the knees, in front of the elbows, and around the wrists, or sometimes on the arms and legs (Fig. 8). There may be some vesiculation and oozing, but this is most likely to have been caused by scratching (the itching is intense); for the essential nature of the process is one of infiltration rather than of vesiculation, chronic rather than acute. It occurs in children who have had eczema in infancy, and who may have been free from it for some time until it begins anew in the locations mentioned. It has been called "neurodermite," a term to which some dermatologists adhere and some do not, and there has been a great deal of argument as to what its exact nature may be. As I have seen it, it almost always occurs in children who have had

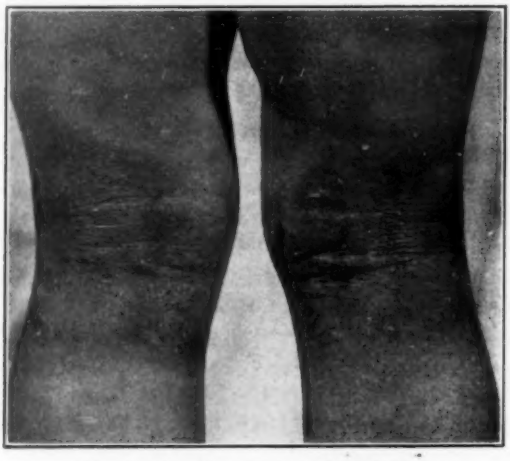

Fig. 8.—Chronic eczema. Lichenification.

eczema as infants, and who were at that time allergic. It is probably best termed "chronic eczema." Skin reactions to food proteins in these children may be negative or positive. Although I have seen many who reacted to egg, removal of egg from the diet is not likely to do much good. As far as dietary regulation is concerned, I do not know of any especial form of diet that is of value in treatment, unless there happens to be specific food sensitization. Withdrawal of supposedly offending foods is not, however, always followed by improvement.

These cases are very rebellious; the thickening is hard to get rid of; the inflammation is controlled for a period and then breaks out anew. A very considerable amount of the trouble is caused by itching, with its consequent scratching, and if it were possible to control this for several weeks, the skin condition would not be difficult to cure. We have had a

number of these children in bed in the hospital ward, and they have uniformly done well—much better than I have seen any do at home. I have a feeling that bed for a period is a very good thing for them, but is somewhat difficult of accomplishment, for they are not sick, and unless the skin condition is very troublesome, the mother is not willing to go to the bother of keeping them in bed.

We are dealing here with a chronic, thickened, sluggish process, and strong remedies, with power of absorbing infiltrate, must be used. We have used either tar ointment No. 1, crude coal tar, or Swartz' ointment.

Swartz' ointment:

| | |
|---|---|
| Mercurochrome crystals | gr. x |
| Aquae | ♏ xx |
| Ac salicylic | gr. xx |
| Vaseline | |
| Lanolin | āā 3 i |

If there is any tendency to oozing, tar ointment No. 1 is the best.

These ointments should be rubbed in vigorously twice a day, and bandages are applied around the elbows and wrists. It is next to impossible to keep a bandage in place around the knees; therefore it is well to have the child wear long white cotton stockings. It is necessary to continue treatment for a considerable period of time, and to persist in it for some time after the skin seems nearly normal. This is a stubborn condition to treat, and results are only fair.

"*Erythrodermia Desquamativa.*"—I have seen no form of local treatment that does much good in the treatment of erythrodermia. Tar, or any other strong preparation, is contraindicated. After trying many salves, washes, and liniments, I have come to the conclusion that nothing is any better than boric ointment applied liberally and frequently. This keeps the skin soft, helps to remove scales and, by its mild antiseptic action, to prevent infection.

## Looking Forward

The problem of infantile eczema is not yet solved, although little by little it is becoming less obscure.

No real progress will result until we can do two things:

1. Make a much more definite separation of the various skin conditions in infancy now called "eczema."

2. Have some means at our command by which we can change an allergic infant into one who is not allergic.

Both are possible of attainment.

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# THE INSTITUTIONAL MORTALITY AND MORBIDITY OF INFANTILE ECZEMA

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RECENTLY, attention has again been focussed on the dangers of the infant ward—its high mortality and morbidity.[1] Both are largely the result of upper respiratory infections and digestive disturbances universally present in infant wards.

On this account, many have come to feel with Brennemann that "no infant should be admitted to an infant ward who can with reasonable assurance be taken care of in an out-patient department, or in a good home or foster home." This would restrict hospitalization of infants to emergencies and to those whose illnesses demand either for purposes of diagnosis or therapy a specialized technic that cannot be provided in a home. In order to define more clearly the character of cases that may still be regarded as eligible for hospitalization in an infant ward, it seems important to decide what classes of cases should not be admitted to an infant ward. Brennemann lists as especially to be excluded, "boarders and infants with infections of the upper respiratory tract and gastrointestinal disorders that are not immediately serious."

Inasmuch as the management of infantile eczema presents a problem often regarded as more ideally treated in a hospital, we have gone over the results obtained in the care of 103 cases of infantile eczema admitted to the Milwaukee Children's Hospital. These 103 patients were not selected in particular, as that number represents *all* the infants and children up to two years, who were admitted from August, 1922, to April, 1931, with a diagnosis of infantile eczema. The only cases omitted from this study are those who did not stay in the hospital long enough for any conclusions to be drawn, as they were taken home against the advice of the attending physician. The cases have been divided into two groups: (1) Those infants admitted for treatment of eczema but otherwise in apparently good health, (2) those infants who had miscellaneous complaints besides their eczema.

Admitted for the treatment of eczema alone were 56 infants (Table I). Of these, 23 had an uneventful stay in the hospital, 33 developed complications, a morbidity of 58.9 per cent. There were 10 deaths in this group, a mortality of 17.9 per cent among previously healthy infants admitted for treatment of eczema. Some of the infants had

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TABLE I

INFANTS ADMITTED FOR TREATMENT OF ECZEMA

| HOSP. NO. | DATE OF ADMISSION | DATE OF DISCHARGE | AGE | COMPLICATIONS AND COURSE | RESULT |
|---|---|---|---|---|---|
| 26576 | 3/ 5/31 | 3/16/31 | 1 yr. | Uneventful | Improved |
| 19483 | 2/24/28 | 3/ 7/28 | 1 yr. 2 mo. | Uneventful | Improved |
| 18286 | 1/14/28 | 1/26/28 | 1 yr. 1 mo. | Uneventful | Improved |
| 19851 | 4/17/28 | 5/21/28 | 8 mo. | Uneventful | Improved |
| 20949 | 7/19/28 | 11/ 7/28 | 2 mo. | Uneventful | Improved |
| 18181 | 7/18/27 | 8/13/27 | 8 mo. | Uneventful | Improved |
| 13559 | 12/31/24 | 1/26/25 | 7 mo. | Diarrhea, upper respiratory infection | Improved |
| 12484 | 7/23/24 | 9/ 9/24 | 9 mo. | Uneventful | Improved |
| 12484 | 4/ 7/24 | 5/31/24 | 5 mo. | Upper respiratory infection, bronchopneumonia | Improved |
| 12314 | 2/12/24 | 2/27/24 | 1 yr. 2 mo. | Uneventful | Improved |
| 24877 | 9/30/20 | 2/12/31 | 1 yr. | Upper respiratory infection | Expired |
| 22425 | 6/10/29 | 7/16/29 | 6 mo. | Upper respiratory infection, diarrhea | Expired |
| 19632 | 3/17/28 | 3/23/28 | 4 mo. | Upper respiratory infection, diarrhea | Expired |
| 25914 | 11/21/30 | 11/26/30 | 1 yr. 2 mo. | Uneventful | Improved |
| 21692 | 1/29/29 | 2/24/29 | 1 yr. | Upper respiratory infection | Improved |
| 18325 | 8/ 9/27 | 9/ 7/27 | 3 mo. | Uneventful | Improved |
| 18156 | 8/ 4/27 | 8/10/27 | 1 yr. | Uneventful | Improved |
| 18145 | 7/13/27 | 8/ 4/27 | 5 mo. | Uneventful | Improved |
| 17230 | 1/24/27 | 3/30/27 | 5 mo. | Upper respiratory infection, chickenpox | Improved |
| 11191 | 8/11/22 | 9/ 5/22 | 2 mo. | Uneventful | Improved |
| 12024 | 10/22/23 | 12/30/23 | 6 mo. | Postauricular abscess | Improved |
| 13968 | 3/23/25 | 4/ 4/25 | 3 mo. | Uneventful | Improved |
| 14769 | 12/ 4/25 | 3/22/26 | 7 mo. | Upper respiratory infection | Improved |
| 15536 | 2/15/26 | 3/ 9/26 | 8 mo. | Uneventful | Improved |
| 15585 | 2/25/26 | 4/12/26 | 6 mo. | Upper respiratory infection | Expired |
| 16158 | 7/ 2/26 | 7/21/26 | 2 mo. | Upper respiratory infection | Improved |
| 19670 | 3/22/28 | 4/ 5/28 | 3 mo. | Intestinal intoxication | Expired |
| 20360 | 6/29/28 | 8/ 6/28 | 6 mo. | Diarrhea | Improved |
| 19473 | 2/23/28 | 3/16/28 | 3 mo. | Intestinal intoxication | Improved |
| 12303 | 2/ 7/24 | 3/ 7/24 | 10 mo. | Uneventful | Improved |
| 12257 | 1/22/24 | 4/ 6/24 | 10 mo. | Upper respiratory infection, mastoiditis, abscess of groin | Improved |
| 14829 | 9/15/25 | 11/ 1/25 | 3 mo. | Otitis media, diarrhea, intestinal intoxication | Expired |
| 26357 | 1/26/31 | 3/ 2/31 | 1 yr. | Upper respiratory infection | Improved |
| 23252 | 10/14/29 | 12/ 7/29 | 4 mo. | Upper respiratory infection, pneumonia | Improved |
| 17401 | 2/26/27 | 7/20/27 | 3 mo. | Spasmophilia, upper respiratory infection, furunculosis, cervical adenitis | Improved |
| 17401 | 8/ 2/27 | 9/29/27 | 8 mo. | Upper respiratory infection | Improved |
| 17517 | 3/19/27 | 4/28/27 | 4 mo. | Bronchopneumonia | Expired |
| 17529 | 3/22/27 | 4/ 4/27 | 4 mo. | Bronchopneumonia | Expired |
| 17194 | 1/17/27 | 2/26/27 | 1 yr. 10 mo. | Upper respiratory infection | Improved |
| 14369 | 6/24/25 | 7/17/25 | 5 mo. | Uneventful | Improved |

TABLE I—CONT'D

| HOSP. NO. | DATE OF ADMISSION | DATE OF DISCHARGE | AGE | COMPLICATIONS AND COURSE | RESULT |
|---|---|---|---|---|---|
| 16087 | 6/20/26 | 7/ 9/26 | 5 mo. | Upper respiratory infection | Improved |
| 21388 | 11/27/28 | 12/15/28 | 8 mo. | Upper respiratory infection | Expired |
| 21587 | 1/ 5/29 | 1/26/29 | 4 mo. | Impetigo, pneumonia | Improved |
| 11731 | 5/14/23 | 6/21/23 | 1 yr. 4 mo. | Uneventful | Improved |
| 23799 | 1/10/30 | 3/14/30 | 2 mo. | Otitis media, furunculosis | Improved |
| 21725 | 2/ 5/29 | 4/16/29 | 2 mo. | Diarrhea, furunculosis, upper respiratory infection | Improved |
| 23038 | 9/ 3/29 | 9/20/29 | 2 mo. 1 wk. | Diarrhea | Expired |
| 18327 | 8/ 9/27 | 10/25/27 | 1 mo. | Uneventful | Improved |
| 11365 | 11/ 3/22 | 11/ 6/22 | 6 mo. | Upper respiratory infection | Improved |
| 18368 | 8/15/27 | 8/21/27 | 1 yr. 2 mo. | Uneventful | Improved |
| 15919 | 1/26/27 | 3/21/27 | 1 yr. | Upper respiratory infection | Improved |
| 16917 | 11/20/26 | 12/10/26 | 2 mo. | Uneventful | Improved |
| 11358 | 10/31/22 | 11/29/22 | 1 yr. 1 mo. | Uneventful | Improved |
| 13309 | 10/25/24 | 11/19/24 | 8 mo. | Uneventful | Improved |
| 13146 | 9/17/24 | 11/20/24 | 3 mo. | Impetigo | Improved |
| 21361 | 11/21/28 | 1/14/29 | 1 yr. 7 mo. | Upper respiratory infection | Improved |

SUMMARY OF TABLE I

| NO. CASES | COURSE DURING HOSPITAL STAY | RESULT |
|---|---|---|
| 23 | Uneventful | Improved |
| 10 | Upper respiratory infection | Improved |
| 3 | Upper respiratory infection | Expired |
| 2 | Bronchopneumonia | Expired |
| 2 | Diarrhea, upper respiratory infection | Expired |
| 1 | Diarrhea, upper respiratory infection | Improved |
| 2 | Upper respiratory infection, bronchopneumonia | Improved |
| 1 | Diarrhea | Expired |
| 1 | Diarrhea | Improved |
| 1 | Intestinal intoxication | Expired |
| 1 | Intestinal intoxication | Improved |
| 1 | Upper respiratory infection, chickenpox | Improved |
| 1 | Upper respiratory infection, mastoiditis, abscess of groin | Improved |
| 1 | Upper respiratory infection, diarrhea, furunculosis | Improved |
| 1 | Upper respiratory infection, spasmophilia, furunculosis, cervical adenitis | Improved |
| 1 | Otitis media, diarrhea, intestinal intoxication | Expired |
| 1 | Otitis media, furunculosis | Improved |
| 1 | Impetigo, pneumonia | Improved |
| 1 | Impetigo | Improved |
| 1 | Postauriculor abscess | Improved |

more than one complication, as shown in Table I. Diarrhea or upper respiratory infection were the most common complications.

There were 47 infants admitted for the treatment of eczema in whom there was an additional admission diagnosis (Table II). Thirty-three of these infants had an uneventful course. Twelve infants developed new complications, a hospital morbidity in this group of 25.5 per cent.

TABLE II

INFANTS ADMITTED FOR TREATMENT OF ECZEMA WITH ADDITIONAL COMPLAINTS

| HOSP. NO. | DATE OF ADMISSION | DATE OF DISCHARGE | AGE | ADMISSION DIAGNOSIS | COURSE | RESULT |
|---|---|---|---|---|---|---|
| 24145 | 3/ 5/30 | 3/21/30 | 1 yr. 1 mo. | Eczema, impetigo | Uneventful | Improved |
| 24145 | 4/29/30 | 5/20/30 | 1 yr. 2 mo. | Eczema, upper respiratory infection | Diarrhea | Improved |
| 23886 | 1/25/30 | 2/18/30 | 9 mo. | Eczema, cervical adenitis | Uneventful | Improved |
| 18286 | 2/ 2/28 | 2/21/28 | 1 yr. 1 mo. | Eczema, infected finger | Uneventful | Improved |
| 19851 | 6/12/28 | 6/27/28 | 8 mo. | Eczema, otitis media | Uneventful | Improved |
| 19018 | 12/ 5/27 | 12/22/27 | 1 yr. 1 mo. | Eczema, intestinal intoxication | Otitis media | Improved |
| 19018 | 11/ 2/28 | 1/21/29 | 2 yr. | Eczema, scabies | Uneventful | Improved |
| 19018 | 4/ 5/29 | 4/20/29 | 2 yr. 5 mo. | Eczema, upper respiratory infection | Uneventful | Improved |
| 18106 | 7/ 8/27 | 8/10/27 | 8 mo. | Eczema, impetigo | Uneventful | Improved |
| 16205 | 9/27/26 | 11/24/27 | 3 mo. | Eczema, furunculosis | Diarrhea, otitis media | Improved |
| 18185 | 7/19/27 | 8/ 1/27 | 5 mo. | Eczema, malnutrition | Uneventful | Improved |
| 11777 | 6/ 6/23 | 6/20/23 | 11 mo. | Eczema, impetigo | Uneventful | Improved |
| 14249 | 5/27/25 | 11/29/25 | 10 mo. | Eczema, upper respiratory infection | Uneventful | Improved |
| 26268 | 1/13/31 | 3/22/31 | 2 mo. | Eczema, impetigo | Diarrhea | Improved |
| 24877 | 6/23/30 | 7/19/30 | 1 yr. | Eczema, clubfoot | Uneventful | Improved |
| 22698 | 7/17/29 | 8/ 4/29 | 1 yr. | Eczema, nephrosis(?) | | Expired |
| 25717 | 10/15/30 | 12/20/30 | 2 mo. | Eczema, diarrhea | Uneventful | Improved |
| 25456 | 9/ 9/30 | 9/12/30 | 1 yr. | Eczema, otitis media | Uneventful | Improved |
| 25456 | 9/23/30 | 10/ 3/30 | 1 yr. 1 mo. | Eczema, otitis media | Pneumonia | Expired |
| 19184 | 1/ 7/28 | 2/ 2/28 | 3 mo. | Eczema, diarrhea | Uneventful | Improved |
| 18253 | 7/29/27 | 8/ 9/27 | 6 mo. | Eczema, otitis media | Uneventful | Improved |
| 18702 | 10/10/27 | 10/26/27 | 4 mo. | Eczema, upper respiratory infection | Uneventful | Improved |
| 16773 | 10/21/26 | 11/ 9/26 | 2 mo. | Eczema, diarrhea | Uneventful | Improved |
| 16773 | 12/ 4/26 | 12/11/26 | 4 mo. | Eczema, upper respiratory infection (dating from previous date of discharge from hospital) | | Expired |
| 16782 | 10/23/26 | 11/10/26 | 1 mo. | Eczema, diarrhea | Upper respiratory infection | Improved |
| 16850 | 11/ 5/26 | 11/24/26 | 1½ mo. | Eczema, upper respiratory infection | Uneventful | Improved |
| 16938 | 11/24/26 | 12/26/26 | 2½ mo. | Eczema, diarrhea | Uneventful | Improved |
| 17865 | 5/23/27 | 8/ 9/27 | 5 mo. | Eczema, otitis media | Uneventful | Improved |
| 17259 | 1/28/27 | 2/ 4/27 | 5 mo. | Eczema, pneumonia | | Expired |
| 17042 | 12/13/26 | 3/21/27 | 6 mo. | Eczema, upper respiratory infection | Cervical adenitis, chickenpox; discharged after 3 months' stay; weight 1 lb. 10 oz. less than on admission | |
| 12135 | 12/11/23 | 2/ 7/24 | 1 yr. 3 mo. | Eczema, asthma | Uneventful | Improved |
| 12181 | 12/27/23 | 1/15/24 | 10 mo. | Eczema, upper respiratory infection | Uneventful | Improved |

TABLE II—CONT'D

| HOSP. NO. | DATE OF ADMISSION | DATE OF DISCHARGE | AGE | ADMISSION DIAGNOSIS | COURSE | RESULT |
|---|---|---|---|---|---|---|
| 13238 | 10/23/24 | 11/22/24 | 1 mo. | Eczema, diarrhea | Uneventful | Improved |
| 15874 | 5/ 5/26 | 5/21/26 | 3 mo. | Eczema, upper respiratory infection | Uneventful | Improved |
| 15916 | 5/12/26 | 5/22/26 | 1 yr. 2 mo. | Eczema, upper respiratory infection | Uneventful | Improved |
| 14653 | 1/30/26 | 2/22/26 | 8 mo. | Eczema, otitis media | Uneventful | Improved |
| 14400 | 1/ 6/27 | 1/27/27 | 1 yr. 9 mo. | Eczema, birth injury | Bronchopneumonia | Improved |
| 16995 | 12/ 4/26 | 12/ 9/26 | 1 yr. 5 mo. | Eczema, cervical adenitis | Uneventful | Improved |
| 17426 | 3/ 3/27 | 5/16/27 | 7 mo. | Eczema, spasmophilia | Upper respiratory infection, otitis media | Improved |
| 17556 | 3/27/27 | 4/ 5/27 | 3 mo. | Eczema, upper respiratory infection | Uneventful | Improved |
| 17391 | 2/25/27 | 3/ 2/27 | 8 mo. | Eczema, upper respiratory infection | Bronchopneumonia | Expired |
| 16917 | 12/20/26 | 12/30/26 | 2 mo. | Eczema, otitis media | Uneventful | Improved |
| 16917 | 1/ 6/27 | 5/13/27 | 3 mo. | Eczema, upper respiratory infection | Cellulitis of face, chickenpox | Improved |
| 17050 | 12/15/26 | 12/27/26 | 3 mo. | Eczema, impetigo | Uneventful | Improved |
| 14994 | 10/15/25 | 11/16/25 | 4 mo. | Eczema, upper respiratory infection | Uneventful | Improved |
| 13210 | 9/30/24 | 10/16/24 | 1 mo. | Eczema, hernia | Uneventful | Improved |
| 26298 | 1/17/31 | 3/15/31 | 1 yr. | Eczema, upper respiratory infection | Uneventful | Improved |

SUMMARY OF TABLE II

| NO. OF CASES | ADMISSION DIAGNOSIS | UNEVENTFUL | COMPLICATIONS | RESULT |
|---|---|---|---|---|
| 15 | Eczema, upper respiratory infection | 11 | 1 Cellulitis of face, chickenpox | Improved |
| | | | 1 Cervical adenitis, chickenpox | Improved |
| | | | 1 Bronchopneumonia | Expired |
| | | | 1 Upper respiratory infection dating from date of discharge previous admission to hospital | Expired |
| 7 | Eczema, otitis media | 6 | 1 Pneumonia | Expired |
| 6 | Eczema, diarrhea | 5 | 1 Upper respiratory infection | Improved |
| 5 | Eczema, impetigo | 3 | 2 Diarrhea | Improved |
| 2 | Eczema, cervical adenitis | 2 | | Improved |
| 1 | Eczema, intestinal intoxication | | 1 Otitis media | Improved |
| 1 | Eczema, furunculosis | | 1 Diarrhea, otitis media | Improved |
| 1 | Eczema, infected finger | 1 | | Improved |
| 1 | Eczema, scabies | 1 | | Improved |
| 1 | Eczema, malnutrition | 1 | | Improved |
| 1 | Eczema, clubfoot | 1 | | Improved |
| 1 | Eczema, nephrosis | | | Expired |
| 1 | Eczema, pneumonia | | | Expired |
| 1 | Eczema, birth injury | | 1 Bronchopneumonia | Improved |
| 1 | Eczema, spasmophilia | | 1 Upper respiratory infection, otitis media | Improved |
| 1 | Eczema, hernia | 1 | | Improved |
| 1 | Eczema, asthma | 1 | | Improved |

There were 5 deaths in this series, 3 of which were from complications incurred during their hospital stay. The mortality in this series was 10.6 per cent.

For the entire group of 103 infants, the mortality rate was 14.5 per cent.

## DISCUSSION

Infants with infantile eczema seem particularly susceptible to those infections which are generally prevalent in the infants' ward. The mortality rate of 17.9 per cent in uncomplicated infantile eczema here recorded is higher than the mortality rates recorded by Cutler[2] for acute appendicitis (11.4 per cent), empyema (16.6 per cent), pyloric stenosis (11.1 per cent) or fracture of skull (10.2 per cent). Admitting the advantages of a superior dermatologic technic provided in hospital care, does the increased morbidity and mortality rate justify our jeopardizing the lives of these infants? Eczemas in infancy not only display a particular susceptibility to respiratory tract infections, but their tendency to unexplained sudden death has often been noted. Clinical review of some of these instances indicates that sudden death in eczema may be the result of a massive infection of the respiratory tract following generalized sepsis. Such infections exhibiting the symptoms of sudden collapse without striking localizing signs are not unknown to the pediatrician. It is curious to note that of 15 instances of sudden death collected by Moro,[3] 13 occurred during February, March, and April—months in which upper respiratory infections are more common.

## SUMMARY AND CONCLUSIONS

1. Of 103 patients with infantile eczema treated in an infant ward, 15 died, a mortality rate of 14.5 per cent.

2. Of the 103 cases of infantile eczema treated in an infant ward, 45 developed one or more complications, a morbidity rate of 43.6 per cent.

3. Of 56 infants with infantile eczema admitted for eczema alone, 10 died, a mortality rate of 17.9 per cent; 33 had complications, a morbidity rate of 58.9 per cent.

4. Infants having infantile eczema should not be admitted to an infant ward if they can possibly be treated in a home or foster home, supervised by an out-patient department, utilizing the Speedwell technic of Chapin.

5. Sudden death in infantile eczema may be the result of massive respiratory infection of hematogenous origin.

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2. Cutler, George David: Boston, M. & S. J. **191**: 333, 1924.
3. Moro, Ernest: Ekzema Infantum und Dermatitis Seborrhoides, Verlag Julius Springer, Berlin, 1932.

2018 E. North Avenue.

# AN X-RAY AND CLINICAL STUDY OF THE ACCESSORY SINUSES IN 430 INFANTS AND CHILDREN

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EDWARD J. LORENZE, JR., M.D.
NEW YORK

IT HAS been our habit in the examination of the respiratory system to include the sinuses as a routine procedure, depending largely upon transillumination to determine the condition of these structures. Examination after this fashion in the child was so difficult and so frequently at variance with clinical symptoms that we began proving our light findings by means of the x-ray. Repeatedly cases passed as normal by us and by consulting rhinologists showed definite sinus involvement on x-ray examination. It was experience of this sort that made us feel that an intensive study of the sinuses and sinusitis in children was desirable.

Transillumination we found in children may determine sinusitis which will be verified by the x-ray, but negative findings by transillumination does not exclude sinus disease that may be shown by the x-ray. This is perhaps to be explained by the absence of bone density in the child, to a greater degree probably because of the absence of old sinus lesions, hypertrophies and polypi found in adult patients. Likewise in a child the pathologic sinus content is apt to be more of the nature of a mucous secretion with pus, providing a lesser density than is supplied by the thick, less translucent pus content found in the adult.

The sinuses in 430 children have been radiographically investigated. Among the 430, sinus disease was demonstrated by the x-ray in 296. The ages were as follows:

2 were under one year of age.
35 were from one to three years.
61 from three to five years.
123 from five to nine years.
75 after nine years.

Sinusitis was demonstrated as follows:

The frontals only in 3.
The maxillaries only in 149.
The maxillaries and ethmoids in 121.
The ethmoids only in 21.
The sphenoids in 1.

Read by title before the American Pediatric Society, Rochester, Minn., May 26, 1932.

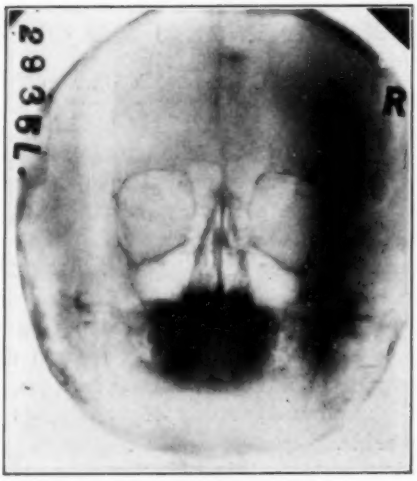


Fig. 1.—E. F., male, aged ten years. Frontals, ethmoids, and maxillaries normal.

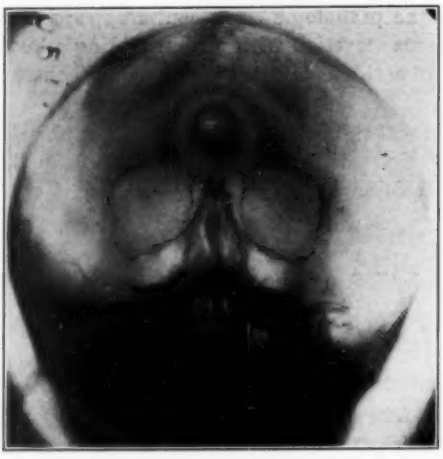

Fig. 2.—M. S., male, aged five years. Normal sinuses.

Among the 296 cases of demonstrated sinusitis, in 215 (72.6 per cent) the tonsils and adenoids had been removed. Obviously, removal of the tonsils and adenoids did not supply protection against sinus infection in these cases.

The complaints for which the children came under observation were:

133 frequent colds.
71 chronic cough and nasal discharge.
31 asthma.
25 rheumatism (recurrent growing pains).
17 persistent slight elevation of temperature.
7 recurrent headache.
4 anorexia.
3 acute coryza.
1 suppurative ethmoiditis.
1 persistent hoarseness.

Fig. 3.—L. B., male, aged five years. Developing sphenoid.

The frontal sinuses were present in various stages of development in 56 of the patients. Seven were between two and three years of age. Five were between three and four years; 10, four and five years; 34 were past the fifth year.

The following cases with roentgenograms have been selected from the group of cases.

Case 1.—E. F., male ten years old, demonstrating normal sinuses for age.
Case 2.—M. S., male five years old, demonstrating normal sinuses for age.
Case 3.—L. B., male five years old, developing sphenoids.

CASE 4.—N. G., female, aged eleven years, strong vigorous girl, applied for treatment because of recurrent head colds for a period of six months, sufficient to interfere with school attendance. Duration of colds about 10 days sneezing and nasal discharge—temperature rarely over 100° F. Tonsils and adenoids had been removed.

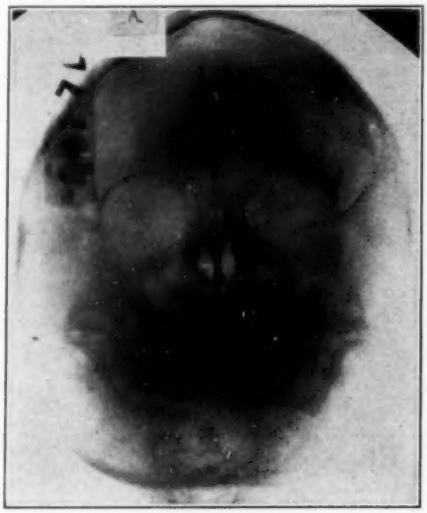


Fig. 4-*A*.

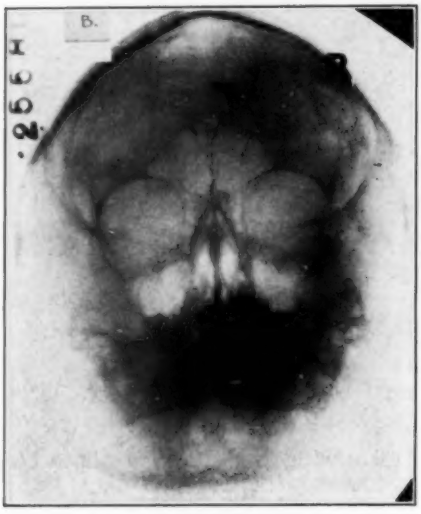


Fig. 4-*B*.

Fig. 4.—N. G., female, aged eleven years. (*A*) Frontals normal, moderate involvement of ethmoids. Involvement of both maxillaries, most marked on right. (*B*) Sinuses clear. Interval twenty-eight days.

CASE 5.—B. W., male, aged seven years, two months, well-nourished boy of average size and weight applied to us because of habitual colds. There had been three attacks in three months each lasting about ten days—profuse nasal discharge, slight elevation of temperature, colds sufficient to interfere seriously with school attendance. Previous winter colds had also been troublesome. Tonsils and adenoids had been removed.

Fig. 5-*A*.

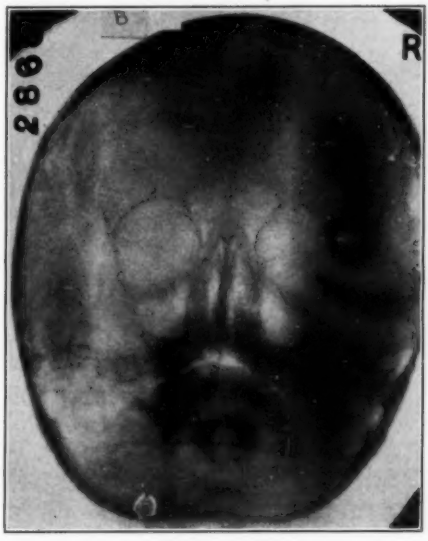


Fig. 5-*B*.

Fig. 5.—B. W., male, aged seven years, two months. (*A*) Frontals clear. Ethmoids and maxillaries blocked. (*B*) Sinuses clear. Interval twenty-eight days.

CASE 6.—S. A., male, aged eight years, well-nourished boy, applied because of persistent hacking cough, profuse nasal discharge for several months. Previous winter same condition reported. Tonsils and adenoids had been removed.

Fig. 6-*A*.

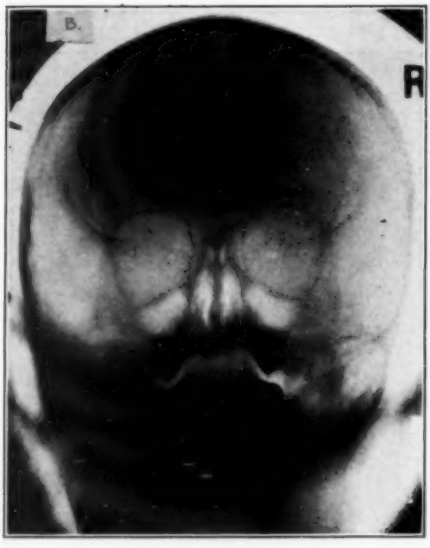


Fig. 6-*B*.

Fig. 6.—S. A., male, aged eight years. Frontals not developed. (*A*) Edema, mucous membrane infiltration of both ethmoids and maxillaries. (*B*) Ethmoids and maxillaries normal. Interval twenty-seven days.

Case 7.—R. M., aged seven years, female, applied for treatment with the history of chronic bronchitis and asthma. Cough most severe in damp weather. Examination of the lungs showed greatly restricted inspiration with fine sharp mucous râles over the chest. Protein skin tests covering fruits, cereals, meats, pollens, vegetables, feathers, hair, fur, eggs and meat were negative. Tonsils and adenoids had been removed.

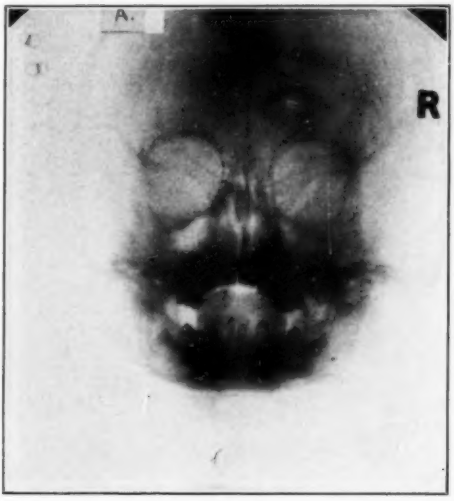


Fig. 7-*A*.

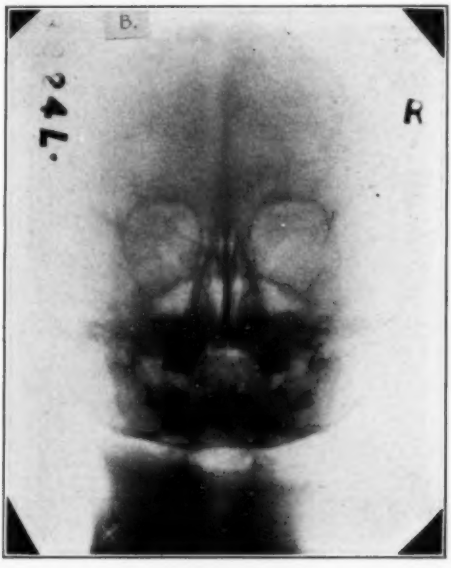


Fig. 7-*B*.

**Fig. 7.—R. M., female, aged seven years. Frontals developing. Ethmoids negative. (*A*) Right maxillary blocked, left edema of the mucous membrane. (*B*) Maxillaries show marked improvement, slight edema of the mucous membrane remaining. Interval thirty-two days.**

CASE 8.—J. M., male, aged four years, 8 months, well-nourished boy had suffered from a cough for nine months, for past three months exceedingly severe particularly at night disturbing patient's sleep and that of the family. The lungs were negative. Tonsils and adenoids had been removed.

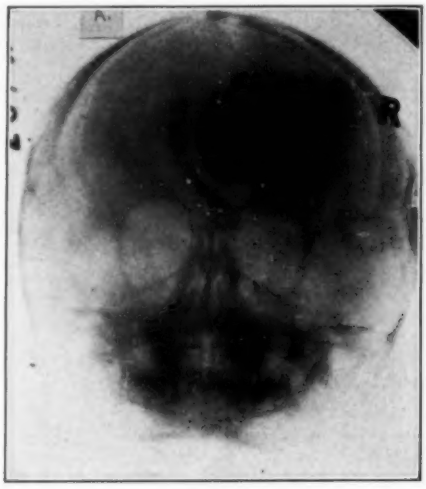


Fig. 8-*A*.

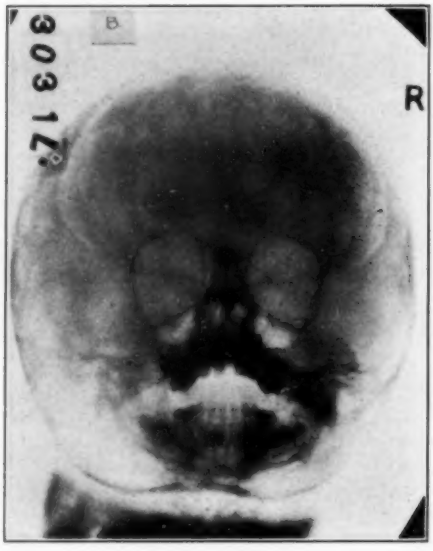


Fig. 8-*B*.

Fig. 8.—J. M., male, aged four years, eight months. (*A*) Frontals absent. Ethmoids show slight involvement. Maxillaries blocked. (*B*) Ethmoids and maxillaries normal. Interval twenty-two days.

CASE 9.—J. S., female, aged six years, six months, frequent colds for one year occurring in rapid succession and associated with marked anorexia. Sinus treatment with cessation of nasal symptoms and normal appetite. Tonsils and adenoids had been removed.

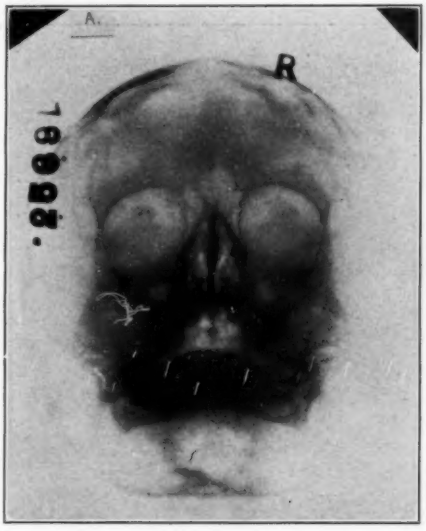


Fig. 9-*A*.

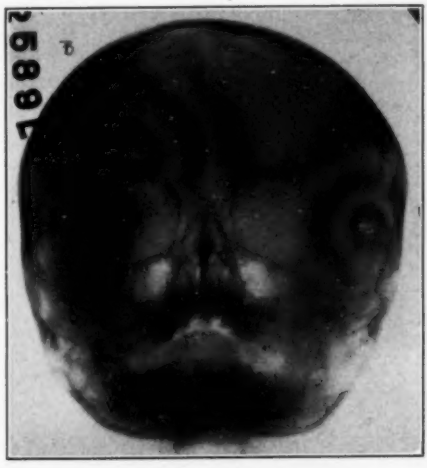


Fig. 9-*B*.

Fig. 9.—J. S., female, aged six years, six months. (*A*) Involvement of maxillaries. (*B*) Sinuses clear. Interval thirty-two days.

CASE 10.—J. R., aged eleven years, female, became ill with acute adenitis followed by severe pain in left eye with protrusion. Temperature 100° to 102° for four days. Clinically acute ethmoiditis. Photographed on fourth day—septum perforated, left maxillary irrigated and drained. Photos—31 days interval. Tonsils and adenoids had been removed.

Fig. 10-*A*.

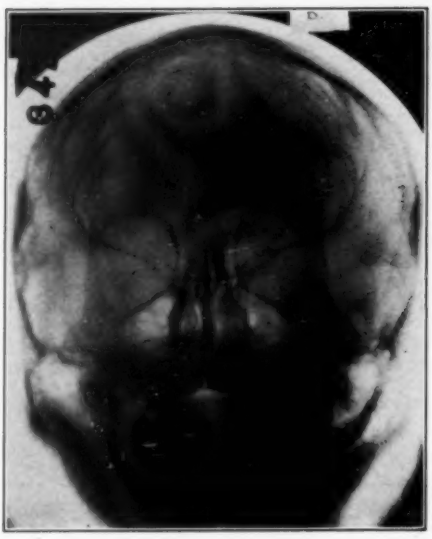


Fig. 10-*B*.

Fig. 10.—J. R., female, aged eleven years. (*A*) Frontals developing. Right ethmoid and maxillary normal. Left ethmoid blocked and maxillary shows extensive involvement. (*B*) Left ethmoid normal. Left maxillary slight mucous membrane involvement of outer border. Interval thirty-one days.

CASE 11.—R. M., female, four years of age, came because of anorexia and periodic elevation of unexplained temperature 100° to 103° for three or four days' duration. Had been treated for acidosis, pyelitis and otitis without relief.

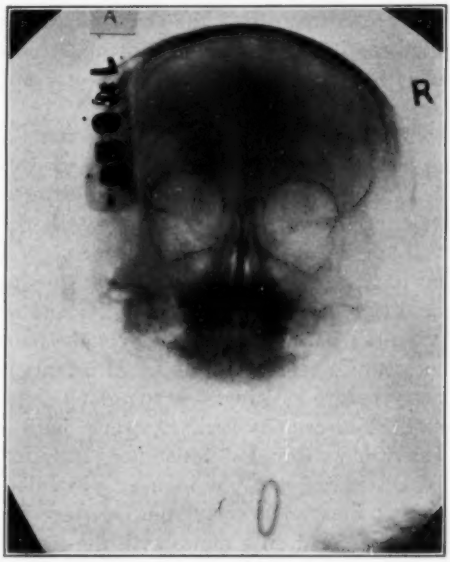


Fig. 11-*A*.

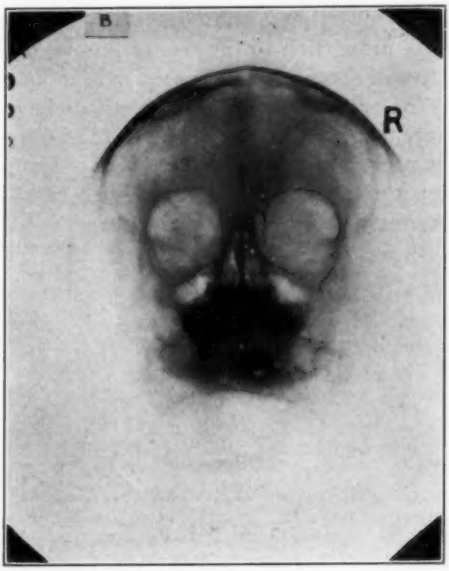


Fig. 11-*B*.

Fig. 11.—R. M., female, aged four years. (*A*) Frontals absent, right ethmoid normal, left developing, extensive involvement of maxillaries. (*B*) Sinuses normal. Interval thirty-four days.

### TREATMENT

We believe that correction of constitutional disorders plays an important part in the management of the child affected with sinus disease. Repeatedly we found it necessary to apply measures for the relief of anorexia, constipation, secondary anemia and to check up faulty life habits.

In two cases with acute ethmoiditis operative procedures were carried out. In all the others nonoperative measures were sufficient to relieve the patient. In five the additional employment of Eggston's stock vaccine was necessary. The treatment was both local and constitutional. Local treatment consisted of 10 per cent argyrol solution on nasal tampons of fifteen minutes' duration at five- to six-day intervals. Morning and evening the nostrils were douched with normal salt solution, employing the Bermingham douche in the older children and instillation by means of a medicine dropper in infants and young children. Immediately before retiring 4 drops of 50 per cent adrephine solution was instilled in each nostril. A warm bath at bedtime followed by a cool shower we found of assistance. In those with a history of profuse nasal discharge, atropin in near physiologic dosage was brought into use. To insure better antrum drainage instructions were given to sleep with the head on a plane with the trunk. This necessitates the absence of a pillow.

We believe that the prompt, satisfactory results which we have had in the vast majority of patients were due in part to the fact that the ostium is larger in proportion to the size of the nasal cavities than in the adult, and to the absence of old pathologic lesions usual in sinusitis of adults. The great majority of our patients have been followed for twelve or more months with few returns of the disorders for which the sinusitis was proved responsible. We believe this to be due to our practice of instructing that every child receive a nasal douche of normal salt solution every day throughout the year.

# TULAREMIA: REPORT OF THREE CASES OCCURRING IN CHILDREN OF THE SAME FAMILY

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University, Virginia

IN CERTAIN sections of this country tularemia can no longer be considered a rare disease. Although the literature contains many interesting and valuable contributions concerning tularemia, but few of these reports are to be found in pediatric literature. The frequency of infection in laboratory workers has been stressed, yet the medical profession and the lay public probably do not yet realize the very infectious nature of tularemia. In order to emphasize this point three cases occurring simultaneously in children of the same family are presented.

Tularemia is an acute infectious disease found primarily in rodents, especially rabbits. McCoy and Chapin in 1912 discovered the causative organism and named it Bacterium tularense. In 1920 Francis isolated the organism from seven human cases and seventeen rabbits and suggested the name tularemia. The organism has been recovered from the blood of infected patients, and from the blood, spleen, and liver of animals dying from the disease. In the majority of cases so far reported, infection followed the handling of infected animals. Infection may also follow fly bite and tick bite.

## REPORT OF CASES

Case 1.—E. C., aged eleven years, was admitted to the Out-Patient Department of the University of Virginia Hospital on March 30, 1932. The following history was obtained from the parents: Twenty-three days before admission to the hospital the child was taken sick with a chill, high fever, and general malaise. Coincident with these symptoms there was noticed an ulcer on the end of the first finger of the left hand. Later the left axillary and epitrochlear glands became swollen and tender. The ulcer on the finger remained sluggish with little tendency toward healing. The child remained quite sick for about two weeks, the illness being characterized by high fever, nausea, vomiting, and at times delirium. The acute symptoms began to subside at the end of two weeks, although the ulcer on the finger and the swollen, tender glands have persisted to the time of admission.

The essential physical findings were as follows: A fairly well-nourished, eleven-year-old boy who did not appear acutely ill. His weight was 74 pounds; the rectal temperature was 99.2° F. On the posterior surface of the first finger of the left hand there was noticed a small, punched-out healing ulcer considerably indurated about its edges. The lesion was not tender. The left epitrochlear and axillary glands were swollen and tender with considerable redness of the skin over these areas. No fluctuation was noticed.

From the Department of Pediatrics, University of Virginia.
Submitted for publication, July 24, 1932.

Laboratory studies were as follows: Hemoglobin 90 per cent (Dare); red blood cells 4,660,000; white blood cells 8,400. Differential count: Neutrophils 52 per cent, eosinophils 1 per cent, basophils 1 per cent, lymphocytes 45 per cent, transitionals 2 per cent. Wassermann, intradermal tuberculin test, and urine were entirely negative. Agglutinations with B. tularense were 4+ to dilutions of 1:320, and 2+ in dilutions of 1:640.

CASE 2.—R. C., aged eight years, was admitted to the University of Virginia Out-Patient Department March 30, 1932, with the following history: Twenty-three

Fig. 1.

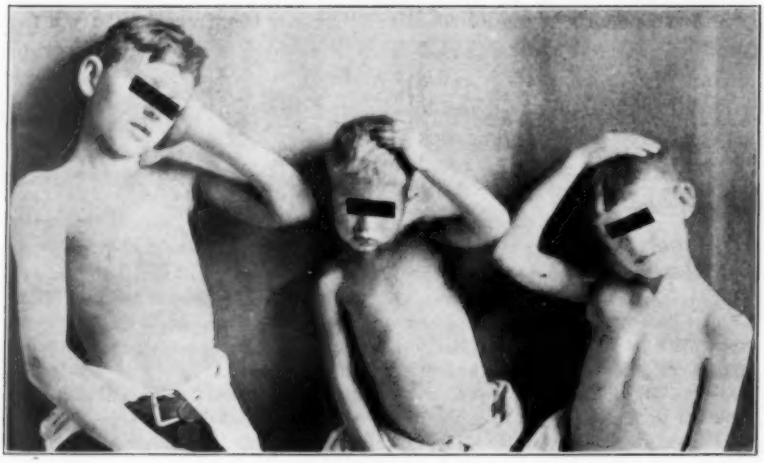

Fig. 2.

days before admission the child complained of pain and tenderness in the right axillary and epitrochlear region. There was also noticed at this time a small ulcer on the right thumb. The patient became rapidly ill with nausea and vomiting, high fever, and delirium. These acute symptoms persisted for two weeks to be followed by gradual improvement. Essential physical findings on admission were as follows: A thin, pale, poorly nourished white boy not acutely ill. His weight was 41¾ pounds, height 50 inches, and the rectal temperature was 99° F. A fluctuant tender mass about the size of a hen's egg was present in the right axilla. A similar

mass about half as large was present in the right epitrochlear region. These masses had the appearance of localized abscesses. On the right thumb there was observed a small red, indurated, healing ulcer.

Laboratory studies were as follows: Hemoglobin 78 per cent (Dare); red blood cells 5,020,000; white blood cells 14,600. Differential count: Neutrophils 57 per cent, eosinophils 1 per cent, lymphocytes 40 per cent, transitionals 2 per cent. Wassermann, intradermal tuberculin test, and urine were entirely negative. Agglutination with B. tularense was 4+ up to dilutions 1:320, 3+ in dilutions of 1:640, and 1+ in dilutions of 1:1280. Treatment consisted of incision and drainage of suppurating axillary and epitrochlear abscesses. Convalescence was uneventful.

CASE 3.—T. C., aged four years, was admitted to the Out-Patient Department of the University of Virginia Hospital on March 30, 1932, with the following history: Twenty-three days before admission the child was suddenly taken ill with nausea, vomiting, chills, and high fever. He complained of pain and tenderness in the left axilla and soon a swollen area appeared in this region. Coincident to these findings a sore on the middle finger of the left hand was noticed. These acute signs persisted for two weeks to be followed by gradual improvement.

Physical examination revealed a well-developed and well-nourished white boy. His weight was 32 pounds, height 39¼ inches, and the rectal temperature 99° F. An indurated, small, healing, punched-out ulcer was noticed on the middle finger of the left hand. In the left axilla there was present a rather firm, tender mass about the size of an acorn. Physical examination was otherwise essentially normal.

Laboratory studies were as follows: Hemoglobin 78 per cent (Dare); red blood cells 4,060,000; white blood cells 13,600. Differential count: Neutrophils 47 per cent and lymphocytes 53 per cent. Wassermann, intradermal tuberculin test, and urine were negative. Agglutinations with B. tularense were 4+ in dilutions 1:80, 3+ in dilutions 1:160, and 2+ in dilutions to 1:640. Treatment consisted of incision and drainage of a left axillary abscess. Convalescence was uneventful.

It is interesting to note that these three brothers all became ill on the same day, and were all similarly affected. There is a definite history of all three children handling a dead ground hog seven days before the onset of their illness. Three days before the acute symptoms appeared these children also killed and skinned a small rabbit. The literature contains references to cases of tularemia occurring following the handling of both rabbits and ground hogs as well as certain other animals and fowls.

## SUMMARY

Three cases of tularemia occurring in three children of the same family are presented. These cases serve well to illustrate the very infectious nature of tularemia.

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Idem: J. Infect. Dis. **10**: 61, 1912.

# THE PRODUCTION AND PREVENTION OF DENTAL CARIES

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PROBABLY the earliest record of the occurrence of dental caries is found in the writings of the Chinese Emperor Huang Ti[1] about 2570 B.C. He divided dental disease into three types: the Fong Ya, or inflammatory conditions; the Chong Ya, or caries, and the Ya Kan, or diseases of the soft investing tissues. Dental disorders, however, were not limited to the ancient Chinese, as the early Egyptians were similarly afflicted. Evidence of this has been obtained both from a study of their ancient inscriptions and from examination of their skulls. Using the latter method, Elliott Smith[2] found that the well-to-do classes that lived on luxurious diets showed dental caries and alveolar abscesses as commonly as Europeans today. The poorer classes that lived on coarse uncooked diets were relatively immune to these diseases. Also, the examination of 364 skulls dating from the Stone Age,[3] which were found in England, reveals the presence of caries in only 64 instances, which would indicate that it was much less common in those far-off times than it is at present. Evidence that dental disease occurred among the Greeks is shown by the writings of Hippocrates (400 B.C.),[4] who supported the idea that toothache was caused by a stagnation of depraved juices in the tooth, and, later, by Aristotle (384-322 B.C.),[5] who suggested, with his remarkable acuity, that the viscous softness of the fig caused small particles to adhere to the gums and insinuate themselves into the dental interstices where they very readily became the cause of putrefactive processes, with resultant damage to the teeth. Unfortunately, there is no statement in the work of these Greek authors on the relative prevalence of the disease. The first suggestion that caries is associated with defective nutrition comes from Galen (second century),[6] who stated that a deficiency of nourishment not only caused the teeth to die away but also enlarged the cavities.

Coming to more recent times, the writings of Krauterman (1732),[7] Bourdet (1757),[8] Bucking (1782)[9] and Tomes (1873)[10] give evidence of the prevalence of caries. During the past twenty years, numerous surveys[11, 12, 13, 14] have indicated that approximately 95 per cent of children suffer from this disease. At the present time there is probably no

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other disease to which the human body is heir that is so widespread or so fraught with potential danger to the health of the individual.

As one would expect, a tremendous amount of work has been done in an attempt to discover the various factors which influence the development of this common disease. In this paper no attempt will be made to discuss this work in detail, as this already has been done adequately by Mellanby,[15] Bunting,[16] Kesel,[17] Hatton,[18] Bing[19] and others, but a brief review of some of the recent work will perhaps not be out of place.

One of the earliest experimental studies on the relation of diet to dental caries was started by May Mellanby[20] in 1917 and is still being carried on. Her results up-to-date have led her to conclude that "the problem of dental caries and periodontal disease is fundamentally a problem of nutrition" and that a lack of vitamin D is an important etiologic factor. Howe[21] reported that by feeding guinea-pigs diets deficient in the fat soluble vitamin (since known to consist of both vitamin A and vitamin D) and the antiscorbutic vitamin, definite lesions in the teeth quite similar to dental caries were produced. The experimental production of carious lesions in the rat analogous to those found in man was accomplished by McCollum and Grieves[22, 23] in 1922 by disturbing the calcium and phosphorus balance in the diet and by giving an insufficient amount of the fat soluble vitamin (vitamins A and D). Toverud[24] was able to cause caries-like lesions in rats by feeding diets low in calcium and fat soluble vitamins. In 1925, Bunting[25] reported that when he reduced the calcium and butter fat in McCollum's stock diet to below that required by the animal, caries-like defects resulted. Marshall[26] reported that similar lesions developed in older rats that were fed diets deficient in fat-soluble vitamins. Shibata in 1929[27] found that dental caries appeared in rats given a diet of rice and greens with 5 to 10 per cent of various sugars, and this was confirmed by Rosebury[28] in 1932. Hoppert, Webber and Canniff[29] state that caries appeared in adequately fed rats when the diet was coarsely ground. Klein and McCollum[30] found that a low phosphorus intake increased susceptibility to caries. Results contrary to those already reviewed were reported by Blackberg and Berke[31] in 1932. They state that when they added extremely large amounts of viosterol to Steenbock's rachitogenic diet (which has a very low phosphorus content) carious lesions developed in young rats after a period of about five months. The amount of viosterol was gradually increased until an amount equivalent to about 60 drams of cod liver oil was fed daily. When a diet high in phosphorus was fed, Klein and Shelling[32] found that excessive doses of vitamin D did not cause caries and therefore concluded that an excessive amount of this vitamin is not a direct cause of the disease.

It is evident that there is marked diversity of opinion as to what is the cause of experimental caries, as a lack of various vitamins, an excess of vitamin D, a deficient supply of the minerals calcium and phosphorus, and the consistency of the food have all been considered etiologic factors in the development of this disease.

Studies on the etiology of human caries have been made by Mellanby,[15] Bunting,[16] Jones,[33] Boyd and Drain,[34] Hanke,[35] Hawkins,[36] Price,[37] McBeath,[38] and others. Mellanby is of the opinion that vitamin D either in the form of cod liver oil or viosterol will prevent caries. Bunting emphasizes the importance of Bacillus acidophilus in the mouth for the production of caries, but believes that "the diet may affect the hygiene of the mouth and the activity of the aciduric bacteria directly through the character of the retained food materials or indirectly through metabolism and alterations in the salivary secretions." He does not consider that any one factor in the diet is responsible for this action. Jones found that diets of children three years of age or older containing fruits and vegetables in amounts sufficient to produce an alkaline ash were invariably associated with sound enamel or arrested decay regardless of how the diet was otherwise constituted. Boyd and Drain believe that the tooth integrity may depend on the adequacy of the diet in *all* essential factors. Hanke states that inflammation of the gums and dental caries either disappear or are greatly alleviated when a pint of orange juice and the juice of one lemon are added to the daily diet. Hawkins found that individuals immune to dental caries consumed liberal amounts of foods which are high in alkaline ash, in calcium and in vitamin D, and low in cereal products. Price believes that dental caries can be largely prevented or controlled by feeding foods sufficiently high in minerals and activators (vitamins). McBeath obtained increased resistance to dental caries by dietary means, but "thus far, however, the superimportance of any one dietary factor has not been demonstrated."

As with the experimental production of caries in animals, human studies also reveal no unanimity of opinion as to the exact cause of this disease. The majority of investigators, however, believe that diet is of great importance in the prevention of caries.

Two of the authors (R. G. Agnew and M. C. Agnew) attempted the experimental production of caries in rats in China in 1927 by feeding a diet low in vitamin D. In 1930, in the University of Toronto, an extensive program was instituted through a joint effort made by the Department of Pediatrics and one of the authors (R. G. A.). In approaching the problem of producing dental caries in animals by nutritional means, it was felt advisable to make as few variations in the diet as possible. It is now recognized that there are at least 37 different elements necessary for normal nutrition;[39] namely, 18 amino acids, one

fatty acid (linolenic acid), glucose, 11 minerals and 6 vitamins. While a lack of any of these substances will interfere with the health of the animal as a whole, the close relationship between certain of these elements and definite pathologic conditions is well recognized; for instance, the relation of iodine to the production of goiter, of vitamin C to scurvy, of vitamin D to rickets, and iron and copper to anemia. It is not unreasonable, therefore, to consider that a limited number of these elements may be intimately connected with the normal nutrition of the tooth, and, conversely, that a lack of these elements may result in the development of certain diseased conditions, including caries.

As the tooth is composed to a large extent of calcium and phosphorus, and as it has been established that vitamin D is essential for the optimal utilization of these elements by the body, our attention was directed particularly to these three elements.

The animals chosen for this work were albino and hooded rats. The ease with which large numbers of these animals can be obtained offers advantages, although they are not ideal animals for our purpose for several reasons. For instance, the rat needs very little vitamin C, which is certainly not the case in man. Also, an exclusive diet of milk will not produce rickets in the rat, but frequently does so in the infant, which indicates that a lack of vitamin D has not such serious consequences for the rat as for man. In addition, the teeth in the rat and in man are not strictly comparable as the former has no deciduous set. Fortunately, however, the twelve molars of the rat are sufficiently similar in structure and function to human molars to make them suitable for experimental study. They are of limited growth, possess deep sulci essentially like those found in human molars, are abraded through mastication in a manner similar to the process of attrition in the human being, and the pulpal reaction to the invasion of the dentinal tubules closely resembles the reaction of adult human teeth.

*Diet No. 1.*—Normal Stock Diet.

| | |
|---|---|
| Calcium content | 0.793 per cent |
| Phosphorus content | 0.496 per cent |

| | *Per Cent* |
|---|---|
| Whole wheat | 60.0 |
| Casein | 14.0 |
| Milk powder | 10.0 |
| Calcium carbonate | 1.2 |
| Sodium chloride | 0.8 |
| Alfalfa | 1.0 |
| Butter | 8.0 |
| Wheat germ | 5.0 |

Spinach or lettuce, 40 grams each week per animal; lean meat, 10 grams each week per animal.

*Diet No. 8.*—Diet normal in Calcium and low in Phosphorus and Vitamin D.

| | |
|---|---|
| Calcium content | 0.612 per cent |
| Phosphorus content | 0.240 per cent |

| | *Per Cent* |
|---|---|
| Cornstarch | 62.0 |
| Casein (alcohol extracted) | 18.0 |
| Crisco (hydrogenated cottonseed oil) | 10.0 |
| Yeast (dry powdered) | 5.0 |
| Salt mixture (Osborne and Mendel's, without calcium or phosphorus) | 2.5 |
| Calcium carbonate | 1.5 |
| Sodium chloride | 1.0 |

Fresh spinach, 100 grams per animal per week, or machine dried alfalfa, 2 per cent by weight.

*Diet No. 8-A.*—Same as Diet No. 8 with 2 per cent of 1D viosterol added.

*Diet No. 11-A.*—Normal Diet.

| | |
|---|---|
| Calcium content | 0.612 per cent |
| Phosphorus content | 0.450 per cent |

| | *Per Cent* |
|---|---|
| Cornstarch | 62.0 |
| Casein (alcohol extracted) | 18.0 |
| Crisco (hydrogenated cottonseed oil) | 10.0 |
| Yeast (dry powdered) | 5.0 |
| Salt mixture (Osborne and Mendel's) | 4.0 |
| Sodium chloride | 1.0 |

To this is added machine dried alfalfa leaf meal, 2 per cent, and 1D viosterol in corn oil, 2 per cent.

*Diet No. 41.*—Diet low in Calcium, Phosphorus and Vitamin D.

| | |
|---|---|
| Calcium content | 0.225 per cent |
| Phosphorus content | 0.260 per cent |

| | *Per Cent* |
|---|---|
| Whole yellow corn (finely ground) | 77.9 |
| Wheat gluten | 20.6 |
| Calcium carbonate | 0.5 |
| Sodium chloride | 1.0 |

*Diet No. 42.*—Diet low in Calcium, Phosphorus and Vitamin D.

| | |
|---|---|
| Calcium content | 0.425 per cent |
| Phosphorus content | 0.260 per cent |

| | *Per Cent* |
|---|---|
| Whole yellow corn (finely ground) | 77.4 |
| Wheat gluten | 20.6 |
| Calcium carbonate | 1.0 |
| Sodium chloride | 1.0 |

*Diet No. 43.*—Diet normal in Calcium (lower limit of normal range) and low in Phosphorus and Vitamin D.

| | |
|---|---|
| Calcium content | 0.625 per cent |
| Phosphorus content | 0.260 per cent |

| | *Per Cent* |
|---|---|
| Whole yellow corn (finely ground) | 76.9 |
| Wheat gluten | 20.6 |
| Calcium carbonate | 1.5 |
| Sodium chloride | 1.0 |

*Diet No. 43-A.*—Diet same as Diet No. 43 with 2 per cent of 1D viosterol added.

*Diet No. 44.*—Diet normal in Calcium (upper limit of normal range) and low in Phosphorus and Vitamin D.

| | |
|---|---|
| Calcium content | 0.825 per cent |
| Phosphorus content | 0.260 per cent |

| | *Per Cent* |
|---|---|
| Whole yellow corn (finely ground) | 76.4 |
| Wheat gluten | 20.6 |
| Calcium carbonate | 2.0 |
| Sodium chloride | 1.0 |

*Diet No. 45.*—Diet normal in Calcium and low in Phosphorus and Vitamin D, with added Vitamins A, B1, B2, C and E.

| | |
|---|---|
| Calcium content | 0.630 per cent |
| Phosphorus content | 0.284 per cent |

| | *Per Cent* |
|---|---|
| Whole yellow corn (finely ground) | 72.5 |
| Wheat gluten | 20.0 |
| Calcium carbonate | 1.5 |
| Sodium chloride | 1.0 |
| Wheat germ | 4.0 |
| Alfalfa (machine dried) | 1.0 |

Tomato juice, 2 c.c. given daily per animal.

*Diet No. 45-A.*—Same as Diet No. 45 with 2 per cent 1D viosterol added.

*Diet No. 46.*—Diet normal in Calcium and Phosphorus and low in Vitamin D.

| | |
|---|---|
| Calcium content | 0.625 per cent |
| Phosphorus content | 0.483 per cent |

| | *Per Cent* |
|---|---|
| Whole yellow corn (finely ground) | 76.0 |
| Wheat gluten | 20.0 |
| Calcium carbonate | 1.5 |
| Sodium chloride | 1.0 |
| Sodium pyrophosphate ($Na_4P_2O_7 + 10H_2O$) | 1.5 |

Diets No. 1 and No. 11-A are normal diets.

Diet No. 8 contains protein of high biologic value and plenty of minerals, with the exception of phosphorus. This diet, however, is also low in vitamin D.

In Diet No. 8-A the deficiency of vitamin D was corrected.

Diets 41, 42, 43, 43-A, 44, 45, 45-A and 46 are modifications of Steenbock's rachitogenic diet[40] which does not contain an optimal quantity of minerals and vitamins, and the proteins are not of high biologic value. Variations were made in this basic diet by changing the concentration of calcium and phosphorus and by the addition of machine dried alfalfa leaf meal, wheat germ and tomato juice. The last three materials add vitamins A, B1, B2, C and E and minerals to the diet.

TABLE I

ABSENCE OF CARIES IN ANIMALS FED NORMAL DIETS

| DIET | AGE OF RATS | NUMBER OF RATS | MACROSCOPIC CARIES | MICROSCOPIC CARIES |
|---|---|---|---|---|
| | *Months* | | | |
| Diet No. 1 | 2 to 5 | 21 | 0 | – |
| Diet No. 1 | 6 to 12 | 138 | 0 | 24 examined, no caries found |
| Diet No. 1 | 12 to 18 | 30 | 0 | – |
| Diet No. 11-A | 2 to 5 | 73 | 0 | 23 examined, no caries found |
| Diet No. 11-A | 6 to 13 | 103 | 0 | 24 examined, no caries found |
| Total | | 365 | 0 | 71 examined, no caries found |

\+ Denotes presence of caries.
0 Denotes absence of caries.
– Not examined microscopically.

The grains used were whole grains which were obtained from the milling companies and then ground in the laboratory. This is important because from experience we have found that one is not certain of receiving whole grains if they are ground by the milling companies. All diets were finely ground three times in a "Hobart" mill and care was taken to ensure adequate mixing of the different ingredients. The 1D viosterol has a vitamin D potency equivalent to that of Steenbock's standard cod liver oil.* It was added in the proper proportions to a quantity of the diet sufficient to last only two or three days in order to avoid possible loss through oxidation which might occur if it were added to a large quantity of the diet and allowed to stand for a long period. The animals were placed on the experimental diets at four weeks of age and were kept in roomy cages which had coarse wire mesh bottoms. Any food that was spilt from the food cups was collected and weighed in order to keep the food records as accurately as possible. No cod liver oil was added to the stock diet of the breeding rats, as it is well recognized that this produces a vitamin D effect in the young which lasts for some time.

After the animals had been fed the diets for stated intervals, they were anesthetized with ether and in some instances blood was taken for the determination of the inorganic phosphorus in the whole blood

*The viosterol used in the animal experiments was furnished through the courtesy of Mead Johnson & Company.

TABLE II

THE EFFECT OF FEEDING DIETS NORMAL IN CALCIUM AND LOW IN PHOSPHORUS AND VITAMIN D ON THE PRODUCTION OF CARIES. RATS NOS. 1 TO 29 FED ON DIET NO. 44 (CALCIUM 0.825 PER CENT AND PHOSPHORUS 0.260 PER CENT), AND RATS NOS. 30 TO 36 FED ON DIET NO. 43 (CALCIUM 0.625 PER CENT AND PHOSPHORUS 0.260 PER CENT)

| RAT NUMBER | PERIOD ON DIET | BLOOD INORGANIC PHOSPHORUS | ASH IN BONES | MACRO. CARIES | MICRO. CARIES |
|---|---|---|---|---|---|
| | *months* | *mg.* | *per cent* | | |
| 1 | 4 | – | 28.5 | + | + |
| 2 | 4 | – | – | 0 | + |
| 3 | 4.5 | – | 30.1 | + | + |
| 4 | 6 | 3.7 | 38.5 | + | + |
| 5 | 4 | – | 24.3 | + | + |
| 6 | 4 | – | 26.3 | + | + |
| 7 | 4 | – | 29.3 | + | + |
| 8 | 4.25 | – | 43.7 | + | + |
| 9 | 4.5 | – | 27.2 | + | + |
| 10 | 4.75 | 1.8 | 34.0 | + | + |
| 11 | 4.75 | 2.6 | 47.3 | + | + |
| 12 | 4.75 | – | 29.5 | + | + |
| 13 | 4.75 | 1.5 | 42.0 | + | + |
| 14 | 3 | – | 22.3 | + | + |
| 15 | 4.25 | – | 27.1 | ? | + |
| 16 | 4 | – | 36.0 | + | + |
| 17 | 4.75 | – | 32.4 | + | + |
| 18 | 5 | – | 29.4 | + | + |
| 19 | 5 | – | 28.0 | + | + |
| 20 | 6 | – | 29.9 | + | ? |
| 21 | 5.75 | – | 26.1 | + | + |
| 22 | 6 | – | 29.4 | + | + |
| 23 | 2.75 | – | – | ? | + |
| 24 | 4.25 | – | – | + | + |
| 25 | 4.25 | – | 24.1 | + | + |
| 26 | 4.25 | – | 29.7 | + | + |
| 27 | 4.25 | – | 35.7 | + | + |
| 28 | 7.5 | 3.2 | 40.0 | + | + |
| 29 | 4.25 | – | 30.3 | + | + |
| 30 | 2 | – | 37.2 | + | + |
| 31 | 2.75 | – | 37.8 | + | + |
| 32 | 2.75 | – | 41.8 | + | + |
| 33 | 4.5 | – | 42.0 | + | + |
| 34 | 4.75 | 5.6 | 32.5 | + | + |
| 35 | 4.75 | 3.5 | 36.6 | + | + |
| 36 | 6 | 2.4 | 50.9 | + | + |

by the method of Fiske and Subbarow.[41] The percentage of ash in the fat free tibia and fibula was also determined, using the Bethke, Steenbock and Nelson[42] technic.

A study of the oral tissues of the animals was made following three general procedures: First, gross study of the teeth and jaws with the aid of the binocular dissecting microscope; second, study of ground undecalcified sections, stained and unstained, of the teeth and the alveolar bone; this included the imbedding method (Kollolith or balsam, which retains the soft tissues *in situ*); third, study of decalcified and serially mounted sections using a variety of stains for tissue or bacterial demonstration.

MACROSCOPIC EXAMINATION

Gross examination revealed lesions of the enamel, dentine (and pulp) which exhibited the characteristics of macroscopic dental caries as seen in the human being. The lesions occurred almost invariably on the occlusal surface, commencing at or near the fundus of the sulci of the crowns. In some cases the external lesion was small in size; in

Fig. 1.—Normal jaw of a rat showing the 6 lower molar teeth (dried). The shadows in the sulci do not indicate pathologic change but are due to the narrow, deep grooves characteristic of the rat molar. Absence of disease was confirmed by subsequent microscopic examination.

Fig. 2.—Carious molar teeth in a rat (dried lower jaw). Note the macroscopic similarity to human occlusal caries as to areas involved and contours of cavities. Note also the absence of cusp fracture or other artefact.

others there was found extensive destruction of a part or of the whole of the crown, exposing the floor of the pulp chamber and the orifices of the root canals. In some instances, weakening of the tooth wall had led to collapse of portions of the crown. Examples of macroscopic caries are shown in Figs. 2 and 3, with contrasting normal conditions in Figs. 1 and 4.

Fig. 3.—Carious molar in upper jaw of a rat. Note extensive loss of occlusal portion of crown uncomplicated by fracture.

Fig. 4.—Molar teeth of a rat (dried lower jaw) free of carious lesions. This rat was fed Diet No. 46, which is normal in calcium and phosphorus but low in vitamin D. The diet of this rat was identical with that used in the case illustrated by Fig. 2, with the exception that phosphorus was added. A similar normal appearance was found in those rats in which no evidence of caries was seen when vitamin D was added but the phosphorus kept at the original low level (Diet No. 43-A). See Table VI.

TABLE III

THE LACK OF PREVENTIVE EFFECT OF ADDITIONAL VITAMINS A, B1, B2, C AND E TO DIET NO. 43 ON THE PRODUCTION OF CARIES. DIET NO. 45 (CALCIUM 0.630 PER CENT AND PHOSPHORUS 0.284 PER CENT)

| RAT NUMBER | PERIOD ON DIET | BLOOD INORGANIC PHOSPHORUS | ASH IN BONES | MACRO. CARIES | MICRO. CARIES |
|---|---|---|---|---|---|
| | *months* | *mg.* | *per cent* | | |
| 1 | 2.5 | – | 38.8 | ? | + |
| 2 | 2.5 | – | – | + | + |
| 3 | 7 | 2.2 | 49.5 | + | + |
| 4 | 2 | – | 48.0 | + | + |
| 5 | 2 | – | 50.3 | + | + |
| 6 | 2 | – | 42.7 | + | + |
| 7 | 2.25 | – | – | + | + |
| 8 | 4 | – | 47.7 | + | + |

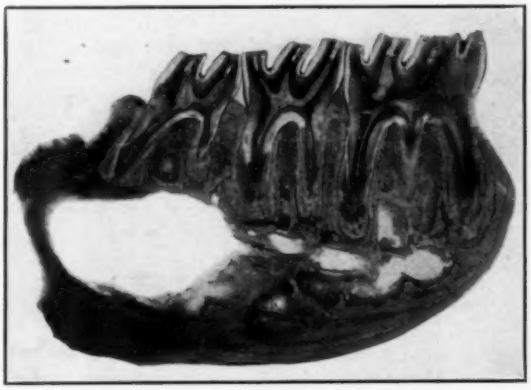

Fig. 5.—Jaw of a rat ground mesiodistally showing the 3 molar teeth of one side free of carious defects. Note the deep narrow sulci between the cusps and the intact enamel.

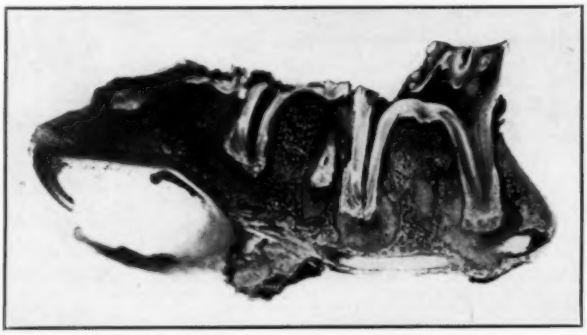

Fig. 6.—Jaw of a rat ground mesiodistally showing results of extensive caries with subsequent collapse of the coronal portions of the teeth.

MICROSCOPIC EXAMINATION

(a) *Ground sections.*—Ground sections again revealed the characteristic phenomena seen in human dental caries. The areas of affected enamel corresponded in location and contour with the areas of affected enamel in human caries where pits, fissures and sulci are attacked. The contours were largely cone shaped, with the base directed toward the pulp and the apex toward the surface of the tooth. Discoloration of the affected enamel corresponded to discoloration of involved enamel in human teeth. Following the penetration of the carious process to the amelodentinal border, secondary caries of enamel, or "backward decay of enamel," was found to occur. This phenomenon consists of a lateral spread of the carious process immediately beneath the enamel, commencing at the point of invasion of the dentine, and is due largely to the abundant anastomosis of the peripheral ends of the dentinal tubules facilitating the spread of the lesion. As a result of this condition, not only is the dentine attacked over a wider area leading to shallow mass collapse of the dentine, but likewise the enamel is attacked from the inner side. Thus, as in the human being, the actual size of the involved area may be considerable, while prior to the col-

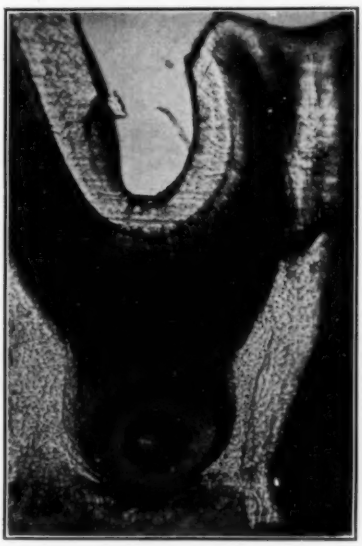

Fig. 7.

Fig. 8.

Fig. 7.—Beginning caries of enamel with discoloration. This is in a very early stage and is unaccompanied as yet by extensive loss of enamel substance.

Fig. 8.—Carious rat molar showing extensive "backward decay" or undermining of enamel. This lesion had commenced at the fundus of the sulcus. Note the portion of enamel in imminent danger of collapse with subsequent wide exposure of dentine.

TABLE IV

THE EFFECT OF FEEDING A DIET LOW IN CALCIUM, PHOSPHORUS AND VITAMIN D ON THE PRODUCTION OF CARIES. RATS NOS. 1 TO 25 FED DIET NO. 42 (CALCIUM 0.425 PER CENT AND PHOSPHORUS 0.260 PER CENT). RATS NOS. 26 TO 35 FED DIET NO. 41 (CALCIUM 0.225 PER CENT AND PHOSPHORUS 0.260 PER CENT)

| RAT NUMBER | PERIOD ON DIET | BLOOD INORGANIC PHOSPHORUS | ASH IN BONES | MACRO. CARIES | MICRO. CARIES |
|---|---|---|---|---|---|
| | *months* | *mg.* | *per cent* | | |
| 1 | 2.5 | – | – | + | + |
| 2 | 2.25 | – | – | + | + |
| 3 | 2.25 | – | – | ? | + |
| 4 | 2.25 | – | – | + | + |
| 5 | 2.25 | – | 39.4 | + | – |
| 6 | 5 | – | 37.6 | + | – |
| 7 | 5 | – | 29.8 | + | – |
| 8 | 5.5 | – | 32.1 | + | + |
| 9 | 6 | 1.5 | 46.1 | + | + |
| 10 | 6 | 1.6 | 42.5 | + | + |
| 11 | 6 | 1.8 | 31.6 | + | + |
| 12 | 2 | – | 35.5 | + | + |
| 13 | 4.75 | 1.6 | 45.9 | + | + |
| 14 | 4.75 | 2.4 | 34.1 | + | + |
| 15 | 4.75 | 3.3 | 35.5 | + | + |
| 16 | 4.75 | 2.3 | 45.9 | + | + |
| 17 | 4.75 | 3.9 | 39.9 | ? | + |
| 18 | 4.75 | 3.5 | 50.0 | + | + |
| 19 | 6 | – | 27.8 | + | + |
| 20 | 4 | – | 49.8 | + | + |
| 21 | 4 | – | 57.8 | + | + |
| 22 | 7.5 | 1.3 | 48.4 | + | + |
| 23 | 7.5 | 2.1 | – | + | + |
| 24 | 7.5 | 2.2 | 54.0 | + | + |
| 25 | 7.5 | 3.0 | 56.0 | + | + |
| 26 | 2 | – | – | + | + |
| 27 | 2.25 | – | 39.4 | + | + |
| 28 | 2.5 | – | 31.6 | + | + |
| 29 | 4.5 | – | 51.8 | + | + |
| 30 | 4.75 | 4.6 | 49.7 | + | + |
| 31 | 4.75 | 3.9 | 41.1 | + | + |
| 32 | 4.75 | 3.1 | 43.5 | + | + |
| 33 | 4.75 | – | 40.2 | + | + |
| 34 | 4.75 | 4.8 | 39.5 | + | + |
| 35 | 2.25 | – | – | + | + |

lapse of the weakened and overhanging enamel the external opening may be minute. In the ground section, moreover, may be seen the phenomenon known as the "zone of translucency," commonly seen in molar occlusal caries in the human being. This is a defensive reaction consisting of a hypercalcification occurring in the involved dentinal tubules, the purpose of which is to wall-off the proximal dentine and the pulp. Figs. 6 to 9 illustrate ground sections of carious rat molars. Fig. 5 illustrates a caries-free jaw for comparison.

(b) *Decalcified sections.*—Decalcified sections afforded much further information regarding the processes involved. Since the organic portion of enamel is relatively very small (approximately 3 per cent), the action of the acids which are formed in the carious process is sufficient to disintegrate the enamel. Similarly, in laboratory decalcification the

enamel is in large part disintegrated and lost unless special imbedding processes are employed to maintain *in situ* the delicate organic matrix. In the case of the dentine, however, the high percentage of organic material present (approximately 28 per cent) maintains the original form and structure even after decalcification. Disintegration and dissolution of the dentine in the carious process are secondarily brought about through peptonization, accomplished by certain proteolytic types of organisms. Naturally, therefore, laboratory decalcification in the preparation of the specimens for microscopic examination reveals further evidence of the structural changes which occur.

Fig. 9.—Ground section of a rat molar showing in the fundus of the sulcus invasion of enamel and involvement of dentine with the production of a defensive "translucent zone" in the dentine, appearing as a light band. Note the deep sulcus filled with débris, also, on the extreme lower left, a similar lesion affecting the cervical portion of the tooth.

In dentinal caries, the matrix is usually decalcified before the tubules are invaded by bacteria. The sheath of Neumann, which forms the immediate wall of the tubule, becomes thickened, and there is an actual increase in the diameter of the tubule. The softened matrix between the tubules is compressed and with peptonization of this matrix and increase in tubular diameter, these tubules may come into contact. These enlarged and prominent "pipe-stem tubules" are readily observed in the sections.

Microorganisms invade the tubules and bring about the disintegration of the sheath of Neumann, thus bringing neighboring tubules into

TABLE V

THE EFFECT OF ADDING PHOSPHORUS TO A DIET LOW IN PHOSPHORUS AND VITAMIN D (DIET NO. 43) ON THE PRODUCTION OF CARIES. DIET NO. 46 (CALCIUM 0.625 PER CENT AND PHOSPHORUS 0.483 PER CENT)

| RAT NUMBER | PERIOD ON DIET | BLOOD INORGANIC PHOSPHORUS | ASH IN BONES | MACRO. CARIES | MICRO. CARIES |
|---|---|---|---|---|---|
| | *months* | *mg.* | *per cent* | | |
| 1 | 2.75 | – | 49.8 | 0 | 0 |
| 2 | 6 | 1.6 | 54.6 | 0 | 0 |
| 3 | 6 | 3.1 | 56.6 | ? | + |
| 4 | 6 | 3.4 | 55.6 | 0 | 0 |
| 5 | 6 | 2.6 | 56.2 | 0 | + |
| 6 | 6 | 3.3 | – | 0 | – |
| 7 | 6 | 2.2 | 48.5 | 0 | ? |
| 8 | 5.5 | – | – | 0 | 0 |

TABLE VI

THE EFFECT OF ADDING VITAMIN D TO A DIET LOW IN PHOSPHORUS AND VITAMIN D (DIET NO. 43) ON THE PRODUCTION OF CARIES. DIET NO. 43-A (CALCIUM 0.625 PER CENT AND PHOSPHORUS 0.260 PER CENT). DURATION OF DIET 2 TO 5 MONTHS

| NUMBER RAT | PERIOD ON DIET | PER CENT ASH IN BONE | MACRO. CARIES | MICRO. CARIES |
|---|---|---|---|---|
| | *months* | | | |
| 1 | 2.5 | 42.4 | 0 | 0 |
| 2 | 3 | – | ? | 0 |
| 3 | 2.5 | 41.2 | 0 | 0 |
| 4 | 3 | – | 0 | 0 |
| 5 | 5 | – | 0 | 0 |
| 6 | 5 | – | 0 | 0 |
| 7 | 3.5 | 54.0 | ? | + |
| 8 | 3.5 | 55.4 | ? | + |
| 9 | 4.5 | 51.2 | + | + |
| 10 | 3 | 46.5 | + | + |
| 11 | 3 | – | 0 | + |
| 12 | 3.5 | 54.3 | 0 | + |
| 13 | 4.5 | 58.5 | + | + |
| 14 | 3 | 49.4 | + | + |
| 15 | 2.5 | 49.6 | + | + |
| 16 | 3.5 | 56.1 | ? | + |
| 17 | 4 | 49.0 | ? | + |
| 18 | 4.5 | – | 0 | + |
| 19 | 3.5 | – | + | + |
| Total 19 | — | | | |
| Average age | 3.5 | | | |

intimate relationship. The term "liquefaction foci" is applied to broadened zones along the course of the tubules where the intervening walls have been broken down.

With increase in size of these "liquefaction foci" and coalescence of neighboring foci, there occurs the gradual production of a cavity in which may be found detritus of dentinal origin with bacteria, etc. Where the "backward decay of enamel" has been extensive, and broad areas of dentine become involved, the contour of the carious area is roughly that of a cone with the apex directed toward the pulp.

A barrier, of variable effectiveness, is often thrown up by the pulp. This overlies the pulpal extremities of the affected dentinal tubules in the so-called "dead tracts,"[43] i.e., the area of involved dentine in which hypercalcification has not taken place, or has been overcome, and this secondary dentine attempts to protect the pulp tissue from peripheral

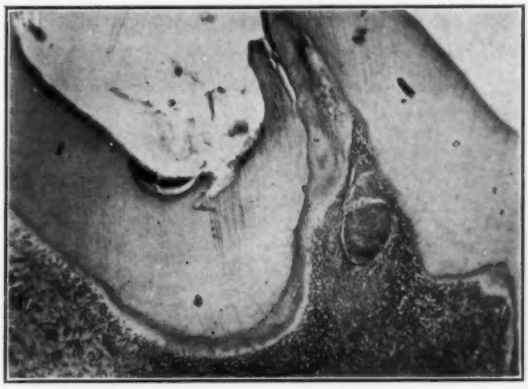

Fig. 10.—Early carious lesion in the dentine of a rat molar (decalcified section). The attack has commenced at the fundus of the sulcus. Note the superficial mass collapse of the dentine and the small number of engorged "pipe-stem tubules" with bulbous enlargements.

Fig. 11.—Advanced stage of caries of dentine in a rat molar. Note the grossly enlarged "pipe-stem tubules" and, particularly in the central portion of the picture, extensive coalescence of "liquefaction foci" with collapse of dentine. Note also the barrier of secondary dentine below this latter area temporarily retarding the process. Note similarity to human condition pictured in Fig. 12.

injuries sustained by the primary dentine by means of a nontubular barrier. (Simple extension of primary dentine does not show this barrier.)

Figs. 10 to 13 are serial sections of decalcified carious teeth showing the process above described.

Fig. 12 illustrates a case of human dentinal caries which shows the similarity to that of the rat.

Control animals have in no instance exhibited evidence of carious lesions. The possibility of the production of caries-like lesions through splitting of the cusps of rat molars or other traumata, with resultant "holes" of noncarious origin, is eliminated by the careful histologic examination. Such splitting of cusps may be observed to a certain extent in both control and experimental animals, but in the control animals has in no case been associated with dental caries.

Fig. 12.

Fig. 13.

Fig. 12.—Caries of dentine in a human tooth showing "pipe-stem tubules" and coalescing "liquefaction foci" and extensive superficial destruction of dentine. Note similarity to Fig. 11.

Fig. 13.—Carious process in a rat molar penetrating the secondary dentine barrier and leading to necrosis of the adjacent pulp tissue. Note the extensive surface loss of dentine. Infected tubules leading from the periphery of the dentine at a further point in the serial are seen to penetrate the secondary dentine along the pulpal wall, causing invasion of the pulp.

## COMMENT

The caries which occurred in these rats is essentially comparable to that found in man. When the animals were fed the normal stock diet No. 1, or the normal diet No. 11-A, caries was never found, even after a period of eighteen months. In contrast to this, the animals which were given a diet composed of yellow corn, wheat gluten, calcium carbonate and sodium chloride, which diet is very low in phosphorus and vitamin D, for two months or more, developed caries in almost every instance. The addition of vitamins A, B1, B2, C and E to this diet

TABLE VII

THE EFFECT OF ADDING VITAMIN D TO A DIET LOW IN PHOSPHORUS AND VITAMIN D (DIET NO. 43) ON THE PRODUCTION OF CARIES. DIET NO. 43-A (CALCIUM 0.625 PER CENT AND PHOSPHORUS 0.260 PER CENT). DURATION ON DIET OVER 5 MONTHS

| RAT NUMBER | PERIOD ON DIET | BLOOD INORGANIC PHOSPHORUS | ASH IN BONES | MACRO. CARIES | MICRO. CARIES |
|---|---|---|---|---|---|
| | *months* | *mg.* | *per cent* | | |
| 1 | 6.5 | 2.9 | 55.8 | + | + |
| 2 | 6.5 | 3.5 | 55.4 | + | – |
| 3 | 6.5 | 3.4 | 55.7 | + | – |
| 4 | 6.5 | – | 43.8 | + | + |
| 5 | 6.5 | – | 55.9 | + | – |
| 6 | 7.5 | 3.0 | 58.1 | + | + |
| 7 | 7.5 | 3.6 | 58.4 | + | + |
| 8 | 7.5 | 3.3 | 59.1 | + | + |
| 9 | 8 | 3.3 | – | + | + |
| 10 | 8 | 3.7 | – | + | + |
| 11 | 8 | 3.7 | – | + | – |
| 12 | 8 | 3.8 | – | + | – |
| 13 | 8 | 4.1 | – | + | – |
| 14 | 8 | 3.5 | – | + | – |
| 15 | 8 | 3.5 | – | + | – |

TABLE VIII

THE EFFECT OF FEEDING A DIET NORMAL IN CALCIUM AND LOW IN PHOSPHORUS AND VITAMIN D ON THE PRODUCTION OF CARIES. DIET NO. 8 (CALCIUM 0.612 PER CENT AND PHOSPHORUS 0.240 PER CENT)

| RAT NUMBER | PERIOD ON DIET | BLOOD INORGANIC PHOSPHORUS | ASH IN BONES | MACRO. CARIES | MICRO. CARIES |
|---|---|---|---|---|---|
| | *months* | *mg.* | *per cent* | | |
| 1 | 5.5 | – | 53.5 | 0 | + |
| 2 | 9.5 | – | 58.7 | 0 | + |
| 3 | 9.5 | – | – | 0 | ? |
| 4 | 9.5 | – | – | 0 | + |
| 5 | 6 | 3.0 | 56.2 | 0 | + |
| 6 | 6 | – | 55.8 | 0 | 0 |
| 7 | 9.5 | – | 56.1 | 0 | + |
| 8 | 13 | 2.6 | 59.0 | 0 | ? |
| 9 | 13 | – | 56.6 | 0 | 0 |
| 10 | 6 | – | – | 0 | 0 |

TABLE IX

THE EFFECT OF ADDING VITAMIN D TO A DIET LOW IN PHOSPHORUS AND VITAMIN D (DIET NO. 8) ON THE PRODUCTION OF CARIES. DIET NO. 8-A (CALCIUM 0.612 PER CENT AND PHOSPHORUS 0.240 PER CENT)

| RAT NUMBER | PERIOD ON DIET | BLOOD INORGANIC PHOSPHORUS | ASH IN BONES | MACRO. CARIES | MICRO. CARIES |
|---|---|---|---|---|---|
| | *months* | *mg.* | *per cent* | | |
| 1 | 6 | 5.0 | 58.6 | 0 | 0 |
| 2 | 13 | 4.4 | 59.8 | 0 | 0 |
| 3 | 13 | 4.4 | 59.7 | 0 | 0 |
| 4 | 13 | 3.9 | 62.1 | 0 | 0 |
| 5 | 10 | – | – | 0 | 0 |
| 6 | 8 | – | – | 0 | 0 |
| 7 | 8 | – | – | 0 | 0 |
| 8 | 8 | – | – | 0 | 0 |
| 9 | 8 | 4.7 | 59.7 | 0 | 0 |

apparently did not influence in any way the development of caries.

As this diet is also deficient in minerals and high quality proteins, one could not conclude from these experiments that the caries was due entirely to the low phosphorus content and the absence of vitamin D. However, when the phosphorus level of this diet was brought up to the so-called normal level, caries was prevented in 4 out of 7 animals for periods up to six months. Also, when the phosphorus was left at the original low level, the addition of vitamin D reduced the prevalence of caries, as 6 (31 per cent) of a series of 19 animals did not develop the disease in periods up to five months.

When we examined the animals fed diet No. 8, which although low in phosphorus and vitamin D is quite adequate in both proteins and other minerals, we found caries in only 50 per cent during periods up to thirteen months. When vitamin D was added to this diet, caries did not develop in a single instance during similar periods.

Calcium was added in varying amounts to give percentages varying from the high normal level of 0.825 per cent to the very low level of 0.225 per cent, but this had no apparent influence on the development of caries.

Other investigations carried on in this laboratory by Dr. Chant Robertson and her coworkers indicate that when the proteins are not of a high grade, or when certain of the vitamins are absent, the resistance to infection and the general health of the animal are impaired. It is quite reasonable therefore to consider that the maintenance of normal teeth is dependent primarily on a sufficient supply of phosphorus and vitamin D, but that any other deficiency in the diet which impairs the general health of the animal would accentuate the effect of the inadequate supply of phosphorus and vitamin D. It is quite possible of course that the consistency of the food might also be a factor in the production of caries in these animals, because the corn diets impacted much more readily than did diet No. 8. It should be noted, however, that when an adequate amount of phosphorus or vitamin D was added to the diet, which did not alter its consistency in the slightest degree, the development of caries was prevented or delayed.

No relation is evident between the percentage of bone ash and the incidence of caries. The whole blood inorganic phosphorus, however, was low in the animals that developed caries. The blood phosphorus of the animals on the normal stock diet No. 1 and the normal diet No. 11-A was usually above 5.0 mg. per 100 c.c. of blood. However, in the older animals, it was sometimes as low as 4.0 mg. and occasionally it even went down to 3.5 mg. A rather unexpected result was seen in the animals receiving added phosphorus (Table V), who although they did not develop caries still showed a low blood phosphorus. The

same low blood phosphorus was found in the animals which were given vitamin D in addition to this diet. Further work will be undertaken on this aspect of the problem.

From our results, it is reasonable to conclude that in the rat adequate supplies of phosphorus and vitamin D are factors in the prevention of dental caries. This is essentially in accord with the views expressed by McCollum and coworkers[22, 23, 30] who stressed the possible importance of these elements as long ago as 1922. In the rat, it is evident that of these two elements the phosphorus is the more important. This is also true in the experimental production of rickets, as this disease cannot be produced in the rat when phosphorus is added to a rachitogenic diet in spite of a low vitamin D intake. However, in infants it is universally recognized that vitamin D is essential for the prevention of rickets in spite of a large phosphorus intake. It is reasonable to expect therefore that in view of the prevalence of caries in individuals who are consuming diets which contain fairly large amounts of phosphorus, the vitamin D factor is of greater importance for the prevention of caries in the human being than it is in the rat.

It is realized fully that the value of this work lies in its application to man. Accordingly, a total of approximately 350 children on diets containing varying amounts of calcium, phosphorus and vitamin D have been observed during the past year in four institutions with the aid of a group of Toronto dentists. A most meticulous dental examination was carried out at the beginning of the investigation and will be repeated at its conclusion. During the period of the investigation the children have been divided into three groups as follows: (a) the control group, in which no change has been made in the diet; (b) a group who have been given additional vitamin D, and (c) a group who have been given both additional vitamin D and phosphorus. An interim examination has recently been made of the children in groups (a) and (b). To ensure an unbiased interpretation of results, operators in examining the children were unaware of the groups into which the children were classified until all the records were completed. This examination showed in those children who had been given additional vitamin D a definite trend toward a lessened incidence of caries as compared to those who had eaten only the usual normal diet. Moreover, the children with added vitamin D showed that previously existing cavities had been largely arrested. In certain of these arrested cases a definite hardening of the cavity walls was apparent. The general tone of the gingivae and of the mucous membrane of the mouth of these children showed a definite improvement when compared with the gingivae and mucous membrane of those children who had not been given the additional supply of vitamin D.

SUMMARY

1. No evidence of dental caries was found in 365 animals fed the normal diets for periods of 2 to 18 months.

2. Seventy out of seventy-one animals fed a diet low in phosphorus and vitamin D for periods of 2 to 7 months showed dental caries. This diet, composed largely of corn and wheat gluten, is also low in other minerals and vitamins, and the proteins are not of a good quality.

3. The addition of vitamins A, B1, B2, C and E to this diet apparently did not have any effect on the development of dental caries.

4. The addition of phosphorus to this diet prevented the development of dental caries in 4 out of 7 rats when fed for periods of 2¾ to 6 months.

5. The addition of vitamin D to this diet in the form of viosterol prevented the development of dental caries in 6 out of 19 rats when fed for periods of 2½ to 5 months.

6. Ten animals were fed a diet composed of cornstarch, casein, vegetable fat (crisco) and yeast, with added minerals and vitamins for periods of 5½ to 13 months. This diet, although low in phosphorus and vitamin D, is adequate in other respects. Dental caries developed in 5 of these animals.

7. Nine animals fed this diet with the addition of vitamin D in the form of viosterol for periods of 6 to 13 months did not show evidences of dental caries in any instance.

8. The amount of calcium in the diet apparently had no influence on the development of dental caries.

9. A preliminary examination of a number of children under observation indicates the importance of an adequate supply of vitamin D for the prevention of dental caries.

CONCLUSIONS

1. Dental caries can be produced and prevented in laboratory animals at will by dietary means.

2. In the rat, an adequate supply of phosphorus is an important factor in the prevention of dental caries.

3. In the rat, an adequate supply of vitamin D may prevent or delay the onset of dental caries. In this animal, the rôle of vitamin D is not of such great importance as that of phosphorus.

4. In man, the addition of vitamin D to diets previously considered adequate in all respects, including phosphorus, is an important factor in the prevention of dental carics.

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# CONGENITAL ESOPHAGOTRACHEAL FISTULA

## Report of Case Living Thirty-Seven Days on Glucose Intraperitoneally

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CONGENITAL malformations of the esophagus are rare. Reynolds and Morrison[1] report but one case in 16 years of autopsies at Bellevue Hospital. Shukowsky and Baron[2] found one in 50,000 hospital cases. At The Mayo Clinic[3] one case has been autopsied. In this instance a gastrostomy was done and the baby fed through the stomach. The baby lived eight days. Graham[4] has recently reviewed the literature and found but 233 recorded cases.

A classification of congenital anomalies of the esophagus by Phelps[5] gives 9 types:

1. Absence of the entire esophagus.
2. Esophagus represented by a solid cord throughout.
3. Double esophagus.
4. Spasm of esophagus.
5. Diverticula.
6. Esophagotracheal fistula.
7. Cysts.
8. Atresia.
9. Stenosis.

Of all the congenital anomalies of the esophagus the one most frequently found is that of the esophagotracheal fistula. Probably 70 per cent of all congenital esophageal malformations are of this type. The upper end of the esophagus generally ends in a blind sac. The lower segment connecting normally with the stomach has its upper end opening into the trachea about a centimeter above the bifurcation.

Zeit[6] gives the most rational explanation of the embryology of this defect. He states that it is caused by a "faulty embryonic anlage of the lower limbs of the lateral ridges." If the lateral ridges turn dorsally instead of ventrally, the esophagus is left ending in a blind sac, with the lower segment of the esophagus communicating with the trachea above the bifurcation.

Heatly[7] states that no case of this type has lived beyond 14 days. Phelps, however,[5] reports one that lived 18 days. The following case that I am reporting lived 37 days. It is also interesting in that it was nourished solely by glucose intraperitoneally.

The infant was born at Ransom Memorial Hospital, Feb. 24, 1932. Parents healthy. Mother multipara. The other children are normal, and there is no history of anomalies in the family on either side. Delivery was spontaneous after a short easy labor. The baby cried lustily at birth and appeared perfectly normal. She had an unusual amount of mucus in her nose and throat the first twenty-four hours.

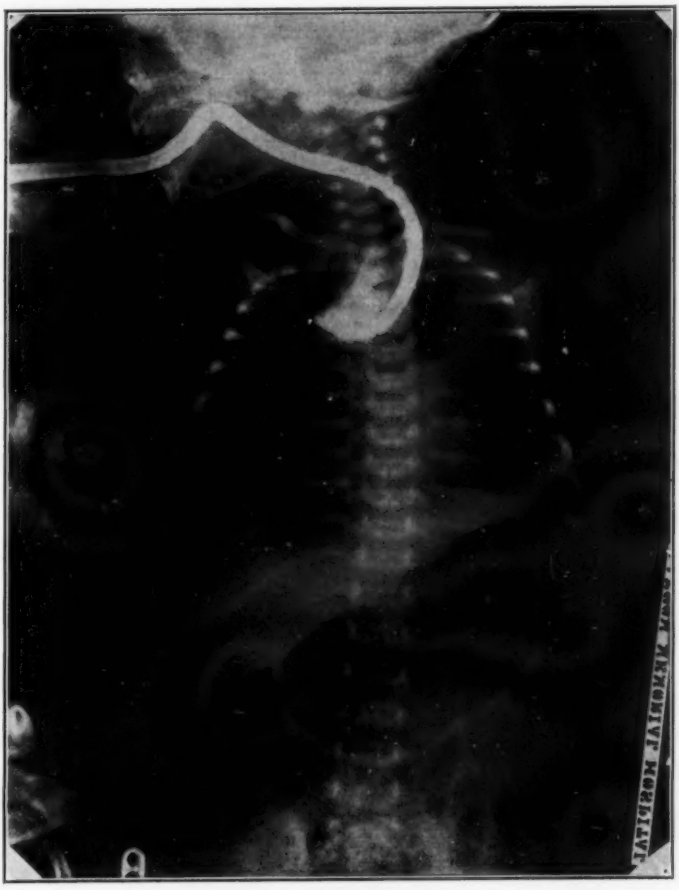

Fig. 1.—X-ray showing catheter and barium in upper end of esophagus.

Physical examination on third day showed a well-developed female baby. Head and fontanelle normal. Left eye pulled in slightly. Heart and lungs negative. Mouth, palate and throat normal. Abdomen normal. Liver and spleen not palpable. Extremities normal. Spine normal. Knee kicks equal and active. Babinski positive on the left side. Definite stiffness of the neck. Pupils react to light.

Because of these findings, spinal puncture was done. Five c.c. of bloody fluid was removed. Six c.c. of father's whole blood was given intramuscularly, and 250 c.c. of 5 per cent glucose solution intraperitoneally. The condition was the

same on the next day, and the spinal drainage was repeated. The following day a third drainage was attempted, but due to extreme rigidity and opisthotonos the canal was not entered. The needle hole at the site of the first abdominal puncture began to bleed, a steady oozing without clotting, and continued several hours. Six c.c. of the father's whole blood was again given in the buttocks. Within two hours the blood was clotting and bleeding stopped spontaneously. There was no further trouble from bleeding. Gavage was now undertaken, but the tube would

Fig. 2.—Drawing of pathological specimen at autopsy.

only go a short distance and meet resistance. It was impossible to pass it into the stomach. A diagnosis was then made of congenital atresia of the esophagus. The baby was given a small amount of barium and a roentgenological examination was made.

Shadow shows esophagus ending abruptly at level of second rib. A catheter was then passed and the x-ray shows it entering the esophagus, meeting the obstruction and starting to turn back (Fig. 1). Lungs inflated; heart shadow normal; considerable gas in stomach. Both pictures show esophagus ending as a blind sac.

The family refused gastrostomy for the purpose of feeding, so the only alternative was nourishing the baby with 5 per cent glucose intraperitoneally. This was done every day with a few exceptions when the fluid from the day before was not entirely absorbed. The first three days Hartman's solution was used to dilute the glucose solution. Then normal saline was used for five days till edema developed in feet, hands and face, due to chloride retention. Distilled water was then used for a diluent and buffer salts added to maintain the blood chemistry.

The baby received 30 intraperitoneal injections of glucose, a total of 8,000 c.c. of solution, averaging about 15 grams of glucose daily, or 60 calories. She was very comfortable and cried less than the average baby. Often an hour or two before injection she would act as though she were hungry. After the needle was inserted she would cry a few moments, then, as the fluid flowed into the cavity, she would nurse her fingers, going off to sleep as a normal baby does when being fed.

Weight at birth, 7 pounds, 13 ounces, dropping to 6 pounds, 13 ounces before glucose feeding were started. Weight at death, 6 pounds. On thirty-seventh day death ensued from bronchopneumonia.

*Necropsy.*—The lungs were inflated and showed bronchopneumonia in both upper lobes. Heart normal. Thymus and thyroid normal. The pharynx, trachea, esophagus and stomach were removed intact (Fig. 2). The esophagus ended as a blind sac at the level of the bifurcation of the trachea. The stomach was connected with the trachea by a tube the size of the normal esophagus, entering the posterior side of the trachea 1 cm. above the bifurcation. The stomach was normal in size and distended with air. A few drops of bile-stained mucus was found at the pyloric end which gave a negative test for glucose. The intestines were collapsed. There was no redness of the peritoneum, but there was a great deal of soft grayish material sticking the loops of bowel together and extending up under the liver and stomach. This, no doubt, was due to a sterile peritonitis from the irritation of the glucose solution. Liver and spleen normal. Kidneys normal. Brain and spinal cord not examined. There were no other anomalies found.

## SUMMARY

A case of congenital esophagotracheal fistula is reported. Life was maintained for thirty-seven days by the use of intraperitoneal injections of glucose solution.

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# THE LIPOID DEGENERATIVE DISEASES

## Discussion of Infantile Amaurotic Family Idiocy (Tay-Sachs' Disease) and Essential Lipoid Histiocytosis (Niemann-Pick's Disease). Report of Case of Each Type in Gentiles

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THE group of what might be called the lipoid degenerative diseases affords a fascinating field of study. The group may be made to comprise (1) infantile amaurotic family idiocy (Tay-Sachs' disease); (2) juvenile amaurotic family idiocy; (3) essential lipoid histiocytosis (Niemann-Pick's disease) and (4) Gaucher's disease. One finds intimations in the literature that Tay-Sachs' disease and the juvenile type of amaurotic idiocy represent respectively the infantile and the juvenile types of a common condition, while Niemann-Pick's disease and Gaucher's disease are similarly related, as parts of another common condition. Bernard Sachs[1] suggested such a possibility. If this idea could be generally accepted it would help to simplify the study of these conditions. However, the opinions of many writers are not, at present, in accord about this matter. The author is interested chiefly in the infantile conditions, viz.: Tay-Sachs' disease and Niemann-Pick's disease. This discussion deals only with these two conditions.

The first case of infantile amaurotic family idiocy was reported before the Ophthalmologic Society of the United Kingdom in 1881 by Warren Tay, an Englist oculist. It occurred in a year-old Jewish child. Sachs read a paper before the American Neurological Association in 1887 in which he reported a similar case in a girl who died at two years. He called it amaurotic family idiocy. Heigers suggested the name Tay-Sachs' disease which met with ready acceptance. It has been generally recognized as a clearly defined condition since that time. The other condition, described by Niemann in 1914 and later studied by L. Pick, is known as essential lipoid histiocytosis, or Niemann-Pick's disease.

The etiology of these conditions has not yet emerged from the state of conjecture. Schaffer[2] says that both are constitutional congenital and familial diseases characterized by a predisposition for the Jewish race. According to him each represents an inherent weakness—"abiogenesis" or "abiotrophy"—of one germ layer; Tay-Sachs' disease being endogenous to the ectodermal layer and Niemann-Pick's disease to the mesodermal layer. Bernard Sachs, as quoted by Wascowitz,[3] expressed the belief that in both conditions the underlying process is a

lipoidal cellular degeneration. In Tay-Sachs' disease the pathology is limited to the central nervous system; in Niemann-Pick's disease it develops as a universal lipoid degeneration in which the reticuloendothelial system assumes an important rôle and in which the nervous system may be involved to a varying degree or not at all.

## PATHOLOGY

Since Tay-Sachs' disease involves only the tissues derived from the ectoderm, the primary pathology is limited to the nervous system. The pathology is so well described by Winkelman[4] in autopsy reports on two cases that I make use of his description. The brain was found to be larger than normal and as firm as if it had been hardened in formaldehyde for weeks. Great variations in the sizes of the convolutions was noted. There was definite thickening of the pia-arachnoid as the result of edema, plus fibroblastic proliferations in the meshes of which were occasional macrophages, but no inflammatory elements. The cortex showed involvement of every ganglion cell. There was a peculiar swelling of the cell body so that many of them resembled a small balloon. There was a disappearance of the normal Nissl body accumulations in the cell body with later accumulations, around the nucleus, of dust-like particles representing the remains of the stainable substance. The rest of the cell body showed a meshwork in the spaces of which lipoid substances could be demonstrated. The nucleus had generally been gradually displaced till it assumed a peripheral position; the nucleus itself showing but mild changes as compared with the cytoplasm. The neurofibrillae were pressed around the margins of the cells. Phagocytic cells were abundant in the intercellular tissues, as were the proliferation of fiber forming astrocytes. The blood vessels appear to undergo little change. This type of pathology is found throughout the ganglion cells of the entire central nervous system.

The idea was advanced by Niemann and Pick that the disease described by them was primarily a metabolic disturbance which resulted in an overloading of the blood and connective tissue with a lipoid material. This stimulates the mobilization of the macrophage system. After saturating the blood and connective tissue the lipoid material invades the tissues of the vital organs and by interfering with their function leads to exhaustion and death. As pointed out by Hassin[5] and others, instead of being limited to the central nervous system the pathologic changes in this condition are practically universal. They may involve the liver, spleen, bone marrow, lymph nodes, lungs, suprarenals, thymus, hypophysis, kidneys, etc., and along with the rest, the brain may be involved. The characteristic histopathologic finding is the so-called foam cell—a large, pale cell containing one or more nuclei and having a vacuolated, honeycombed structure filled with substances

having microchemical properties similar to those present in Tay-Sachs' disease. The origin of these phagocytic cells, or histiocytes was studied by Bloom.[6] He concludes that they come from the resting endothelial and Kupffer cells in the liver; the reticulum cells of the lymph nodes, spleen, and bone marrow, and of the medulla of the suprarenal gland; from the septal cells of the lung and from the wandering cells and phagocytes all over the body. The distribution of the pathology in both cases is in keeping with Schaffer's contention that Tay-Sachs' disease is an endogenous ectodermal condition and Niemann-Pick's disease is an endogenous mesodermal condition. The nature of the lipoid disturbance is not well understood. Some think it is primarily a dysfunction of the endothelial system; others feel that the trouble begins with the cells of the liver and still others that it is an endocrine disturbance. As previously stated, Schaffer holds that each disease represents an inherent weakness of its own particular germ layer.

## SYMPTOMATOLOGY

In studying the symptomatology of the two conditions we find that they have certain things in common. As pointed out by Gauterman,[7] the infants who later develop these conditions are generally born of healthy parents and are themselves healthy and comely specimens. They do well and develop in a normal way up to about the age of six months. At that time, or soon after, it becomes noticeable that the baby is not doing well. It takes less and less food and stops gaining. Development, both mental and physical, is interrupted and it is soon evident that retrogression is taking place. The infant that could hold up its head or perhaps sit alone, soon loses the ability to do these things and becomes helpless. In the Tay-Sachs' type mental impairment gradually leads to idiocy. The muscles of the extremities and trunk become useless—sometimes flaccid and sometimes spastic. The reflexes may be normal, increased or diminished. There is gradual loss of vision till total blindness exists. The ophthalmoscope reveals the characteristic cherry red spot in the region of the macula lutea and later the optic atrophy. Nystagmus or strabismus may be present and hyperacusis is common. There is a marked wasting and death usually takes place before the age of two years. The Niemann-Pick's type presents a somewhat similar picture. Anorexia and vomiting are apt to be encountered earlier and are more troublesome. The liver and spleen become enlarged early, there may be a brownish discoloration of the skin, moderate leucocytosis and moderate to marked anemia. A peculiar vacuolization of the lymphocytes is common and an increase in the lipoid constituents of the blood. A high degree of susceptibility to respiratory infections exists. The eyegrounds may or may not show the cherry red spot. There is apt to be loss of vision with definite optic atrophy.

There is the same mental and physical deterioration as is seen in Tay-Sachs' disease with death resulting before or during the second year from the progressive exhaustion or an intercurrent infection. The pathology being much more general, this condition is more rapidly fatal than is Tay-Sachs' disease.

Both conditions are hereditary, familial and much more common in the Jewish race. Stewart[8] reported a case of Tay-Sachs' disease representing the second generation where six out of twelve children in the previous generation had died of the condition. Some of our fairly recent textbooks still state that amaurotic family idiocy is limited to the Jewish race. Cases seen in gentiles are usually held to be of sufficient interest to be reported. In 1922 Cohen[9] was able to find reports of six cases of Tay-Sachs' disease in gentiles and added one more. In 1930 Greear[10] found nine such cases reported and added one of his own. A case report is here given of each type of disease in non-Jewish families.

CASE 1.—M. A. B. White female, aged nineteen months. Admitted to the hospital on account of convulsions, twitching of the muscles about the mouth and continuous rolling of the head.

She was a full-term baby who appeared to be perfectly well after a normal delivery. The father was thirty-seven years of age and enjoyed reasonably good health, a painter by trade. The mother was twenty-seven years of age and had good health. There had been no previous pregnancies. The parents and grandparents were sure there was no Jewish blood in either side of the family. The father's family were of Irish descent. There was no history of deaths suggestive of amaurotic idiocy among any of the relatives. There was no blood relationship between the parents.

The baby was breast fed and appeared to be healthy and to develop in a normal manner, both physically and mentally. She held up her head at the usual time and sat alone at six months. Dentition was late, the first tooth appearing at one year. At about the ninth month it was noticed that she was becoming listless and taking her food poorly. She progressively lost the use of her muscles and became quite helpless by the time she was sixteen months old. She deteriorated mentally in proportion and began to have convulsions at about sixteen months.

On admission to the hospital she was stuporous. She was fairly well nourished and did not appear anemic. The chest was clear and there was no enlargement of the liver or spleen. The extremities were spastic and there was practically no response to painful stimuli. The pupils were equal—being sometimes dilated and again contracted. There was some lateral nystagmus. The eyegrounds showed the typical light colored area in the region of the macula with the small cherry red spot in the center—diagnostic of amaurotic family idiocy. Optic atrophy was present. A spinal puncture showed no unusual findings and the spinal fluid Wassermann was negative. Her condition grew slowly and progressively worse, but she lived more than a year longer. At times she was rather irritable and was markedly sensitive to noises. Toward the end she became extremely emaciated and swallowed with great difficulty. She died of exhaustion at thirty-four months of age.

NECROPSY (seven hours postmortem).—By Dr. Hugh Jeter. The body is that of a well-developed, emaciated, pale, white, female baby, thirty-four months of age. The anterior fontanel is not closed. Careful exploration and gross examination of

Fig. 1.—Composite picture of Case 1. *A*, 3 months. Holds head up. *B*, 4 months. When lying on stomach raises head and chest in normal manner. *C*, 6 months. Sits up. *D*, 10 months. Holds herself up in normal manner. *E*, 1 year. Beginning to be listless and to slump over. *F*, 13 months. Becoming more helpless. *G*, 16 months. Unable to sit up at all. *H*, 19 months. Loss of use of voluntary muscles.

Fig. 2.—Case 1 at two years. Blind, absolutely helpless and has no mentality.

the lungs, liver, spleen, kidneys, gastrointestinal tract, and genitalia, show no evidence of any pathologic changes, except for generalized anemia. All organs appear to be normal in size.

*Brain.*—Considerable thin watery fluid exudes from the surface of the brain everywhere. The brain is firm, the surface smooth, and regular, and there appears to be no gross anatomic deformities.

*Microscopic Examination.*—Sections from the cortex, medulla, pons, cord, lining of the lateral ventricles, and several other portions of the brain are all remarkably similar, in that there appears to be no important changes except in the ganglion cells. These show evidence of degenerative changes. The outline of the cytoplasm is irregular in most instances which would suggest degenerative changes of the limiting membrane. In some cells the nucleus is eccentrically located. All cells show evidence of pyknosis, karyorrhexia, or karyolysis. The cytoplasm in most of the cells takes a pink stain and in some areas is a much darker pink than the cytoplasm of other cells in that region. There is also some brown pigment deposit in some areas. From the evidence we can obtain by hematoxin and eosin stain of sections from different portions of the central nervous system, it is quite evident that the histopathology is that of amaurotic family idiocy.

Fig. 3.—Case 2. Shows listless, helpless condition. The lower border of the liver is shown and the edema of the lower extremities.

CASE 2.—A. L. B. White male nine months old. Admitted to the hospital because of pallor and listlessness.

He had been a healthy, full-term baby. The father was a ruddy-faced, healthy looking middle-aged man. The mother was rather frail looking but enjoyed reasonably good health. There were five older children living and well and there had been no deaths in the family. There had been no cases of illness similar to that of the patient among any of the relatives. There was no Jewish blood in the family nor any cases of marriage between blood relatives. The baby was breast fed and thrived well for the first few months. He sat alone at six months but from this time on he began to develop a pallor and to become listless and gradually became completely helpless. It became difficult to get him to nurse and he began to develop an edema of the lower extremities.

On admission to the hospital he appeared to be well-developed and nourished but there was considerable edema of the subcutaneous tissues. He looked acutely ill and was very listless. The anemia was so marked the ears were almost transparent. He coughed considerably when disturbed. The two lower central incisors were through and there was a small ulcer on the frenum linguae near its base. The heart was rapid and a soft systolic murmur was heard over the precordium. Numerous coarse, moist râles were heard over both lungs, more marked on the right side. The spleen was enlarged, extended about two inches below the

costal margin and was fairly soft. The liver extended about two inches below the costal margin. The lower extremities were flaccid. The fontanels were closed. Examination of the eyes by Dr. E. S. Ferguson showed the following: pupils react to light and the media clear; optic nerve atrophy on both sides; the macula shows more redness than the remainder of the fundus but there is no definite cherry red spot. An x-ray picture of the chest showed an inflammatory process extending out slightly from both hili. A later picture showed this to be considerably increased on the right side. Several urine examinations revealed no pathology. On admission the blood picture showed: hemoglobin 39 per cent, total erythrocytes 1,490,000, total leucocytes 4600, polymorphonuclear neutrophiles 42 per cent, transitionals 2 per cent, small lymphocytes 40 per cent, large lymphocytes 16 per cent. The erythrocytes showed moderate anisocytosis and poikilocytosis. The leucocytes looked normal. The reticulocyte count was approximately 0.8 per cent. The fragility test was normal. A throat culture showed many staphylococci. Smears from the mouth showed no thrush. The blood calcium was 14.5 mg. and the blood phosphorus 4.64 mg. Blood smears showed no malaria parasites. The spinal fluid first contained blood caused by the needle but was clear at a later time and showed no pathology. The Wassermann reaction was negative on both blood and spinal fluid.

He ran an irregular temperature ranging from normal to 105° F. Repeated blood transfusions brought about satisfactory improvement in the blood picture (the hemoglobin reached 88 per cent and the erythrocyte count 4,450,000) but there was no corresponding improvement in the general condition. He was fed by gavage and given luminal to quiet the nervous irritability. Toward the last practically all food was regurgitated. The pulse steadily became more rapid and weaker and the respirations became more difficult. Death took place nine weeks after admission at the age of 11 months. Autopsy was not permitted.

## COMMENT

The first report is of a clearly defined case of Tay-Sachs' disease in a non-Jewish family verified by autopsy. Some fairly recent textbooks still state that the condition occurs only in Jews. Its onset and development are well illustrated by this case. The statement is commonly made that these patients die during the second year. This child was almost three years old at death.

While an autopsy was not done in the second case it was felt that there were sufficient reasons for making a diagnosis of amaurotic family idiocy of the Niemann-Pick type. The history of onset and progress was typical. The optic atrophy with a reddened area in the region of the macula, made up an important part of the picture. Evidences of involvement of the liver, spleen and bone marrow are characteristic of Niemann-Pick's disease as opposed to Tay-Sachs' disease. The anorexia, vomiting and susceptibility to respiratory infections were characteristic. Reports of the two cases illustrate the fact that Niemann-Pick's disease is more rapidly fatal than is Tay-Sachs' disease. The reports give further proof that neither type of case is confined entirely to the Jewish race.

SUMMARY

A brief discussion of the etiology, pathology, and clinical course of infantile amaurotic family idiocy (Tay-Sachs' disease) and essential lipoid histiocytosis (Niemann-Pick's disease) is presented. Certain points of similarity and certain differentiating characteristics are brought out. A typical case of each condition in non-Jewish families is reported.

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# ANTIQUES OF PEDIATRIC INTEREST

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THE civilization of Egypt was matriarchal in type and no indication of infanticide as practiced by the early Romans is to be found. During its infancy the mother had charge of the child which she nursed for a period of three years. The infant was carried in a shawl slung around the neck of the mother or older sister. During the first four years of childhood the boys, and very often the girls, went nude. Examples of their toys which have been preserved consist of pottery models of household implements and wild and domestic animals, balls

**Ancient Egyptian Toys**
**1. and 2. Toy vases, green glaze, 1000 B.C.**
**3. Kohl or stibium pot, alabaster, 1000 B.C.**
**4. Ball, diameter 5½ cm., green glazed pottery, 100 B.C.**

of rag, leather and pottery, dolls in various materials, tops, and even working models in wood, such as a crocodile whose lower jaw was controlled by a string, and a movable figure of a baker kneading dough. Necklaces, finger rings and bracelets for adornment are common and probably the child painted its eyelashes with stibium in imitation of the mother's practice.

With the beginning of youth, at the fifth year, education commenced. This was superintended by the father. Even at this early age the children of the upper class were frequently sent away to school to be educated in the palace with the royal children, or entered the school belonging to one of the government departments to prepare for an official career. School discipline was severe: "The youth has a back,

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he attends when it is beaten"; "Spend no day in idleness, or thou wilt be flogged. For the ears of the young are placed on the back and he hears when he is flogged." The father counselled his son: "Be not proud of thine own learning, but do thou take counsel with all, for it is possible to learn from all." "Look not around in the house of another, speak not too much, for men are deaf to the man of many words; be silent rather, then shalt thou please; therefore speak not. Before all things guard thy speech, for a man's ruin lies in his tongue. Behave with propriety at meals, and be not greedy to fill thy body. Never forget to be respectful and do not sit while another stands who is older than thou, or who holds a higher office than thou dost." Through education the boy was able to become a government official, therefore, "set to work and become a scribe, for then thou shalt be a leader of men." The food of the schoolboy consisted of three loaves of bread and two jugs of beer daily. The period of youth ended with the sixteenth year.

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# Critical Review

## A REVIEW OF CERTAIN CLINICAL ASPECTS OF NUTRITION

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DURING the past decade, many valuable contributions have been made to the knowledge of nutrition. The medical journals have been unable to keep pace with the articles submitted for publication; during the last few years, new journals pertaining to the field of nutrition and chemistry have been established at the rate of one every two weeks.[1] This new knowledge affects every phase and specialty of medicine; in some instances it is to revolutionize standard habits of thought and practice. Many of the reported researches seem primarily theoretical in their nature, yet the theory of yesterday is finding its direct application today in the interpretation and treatment of disease. This new information has not found its way to any considerable extent into our medical texts; the concepts in many respects are different from those formerly taught in medical courses. The principles of nutrition receive but slight emphasis in the curricula of most of our medical colleges. It is necessary to go to the current literature to obtain information in this field. Fortunately, several excellent journals now are available, devoted to abstracting and discussing the reports of the world literature along these lines.[1, 2] This review is limited to some phases of current thought which should be of special interest to the practitioner of medicine.

At the close of the nineteenth century, the progress which had been made in the fields of organic pathology and bacteriology gave promise that the conquest of disease lay along these lines. These avenues of thought have dominated medical education, often to the point of subordination of the study of applied physiology. It is not surprising that the earlier discoveries in nutrition were interpreted according to these concepts. Thus, when Eijkmann[3] in 1897 demonstrated the value of certain foods in the relief of beriberi, he thought that the effect was one of detoxifying some product ingested or formed in the body. At that time, it was recognized that the food must include certain types of substances, such as had been identified as body components. These consisted of protein, carbohydrate, fat, water and certain mineral salts. Early studies in nutrition were based on observations of living beings whose diets were limited to these constituents. Such feeding experiments were more or less compatible with life and health as long as naturally occurring foods were used. When attempts were made to substitute for these the recognized essentials prepared synthetically, and in relatively pure forms, it was found that experimental animals did

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not make normal progress, and eventually died showing various syndromes of disease. Thus the recognition finally came that these food elements do not in themselves constitute a diet complete for the body's needs, and search was made for the missing substances. Hopkins[4] predicted their existence in 1906; Eijkmann[3] reinterpreted his observations according to this thought about the same time. Funk[5] was the first, in 1911, to isolate such a substance in a relatively pure state, and to which he gave the name, "beriberi vitamin." The terminology was based on the supposed chemical structure of the substance, and its curative and preventive effect in beriberi. He predicted that other substances would be discovered, bearing similar relationship to other diseases of unknown origin. Subsequent investigation has substantiated his prediction; at present not less than thirty-five essentials for normal nutrition are recognized, and it is doubted whether the end has been reached.[6] Conditions described until recently in our medical texts among diseases of unknown etiology, now are recognized as dependent upon specific nutritional deficiencies; the list of such conditions is still growing. More than this: it has been shown that normal health, normal growth and stature, normal longevity, and conditions considered as hereditary or racial characteristics, must be considered as relative terms, since there is much to indicate that what has been accepted as normal for the individual is not necessarily the optimum, and that through suitable measures much may be done to improve upon our formerly accepted standards.

One of the foremost investigators in this field has commented upon the fallacy of accepting averages as standards or norms.. "The mere survival of a community," he states, "is too often taken as proof that the nutrition of its constituent individuals is adequate; lack of health or efficiency being attributed to racial or other uncontrollable factors. In social-economic surveys a race or community is found in equilibrium with an environment which includes its food supply. It is often forgotten that such an environment is fortuitous and that the equilibrium reached is one which the community, while managing to survive, may yet be functioning at levels far below those possible for its innate capacities. . . . With sufficient space it would be easy to show that faulty nutrition has played a large part in inhibiting human progress, and even to show that few races have at any time been ideally nourished. One need not go far back in history to illustrate this. In the most prosperous days of the Victorian era the methods of infant feeding in this country (England) were exceedingly faulty, and had dire results. When the food supplies of existing native races are studied they are often found to be so deficient in certain essentials as to limit the productive capacity of the races in question. . . . Only a couple of generations ago it was supposed that a community in which the crude appetite of all individuals is duly satisfied, and obvious starvation avoided, is a community adequately nourished. Ill-health and inadequate performance in such a community must, it was assumed, be due to causes in which nutrition has no part. We now know that the satisfaction of appetites by mere bulk consumption is no final proof that a food supply is adequate, and this is as true of the animals which we breed for our uses as it is of ourselves. Quality in food is at least as important as quantity; details are of the utmost significance; the absence of factors which add almost nothing to the bulk of a dietary may make the whole entirely inadequate."[7]

Orr and Gilks[8] have reported the results of a prolonged study of two African tribes which exist under similar environmental conditions in Kenya, but whose diet habits are markedly different. This work was done under the auspices of the British Medical Research Council, and appears painstaking and thorough. One group, the Masai, lives for the most part on a diet relatively rich in protein, fat, and calcium, consisting in large measure of meat, milk and raw blood. The other group, the Akikuyu, subsist mainly on cereals, supplemented with roots and fruits; analysis of the dietary shows it to be rich in carbohydrate and in phosphorus, but low in calcium. The full-grown Masai averages five inches taller and twenty-three pounds heavier than the Akikuyu, and his strength is 50 per cent greater. The types of disease seen among the Masai with greatest frequency were rheumatoid arthritis and intestinal stasis, while with the Akikuyu bony deformities, dental caries, anemia, various pulmonary conditions and tropical ulcer were predominant. Parasitic infestation was greater in the latter group. The diets of the young children, the girls and women were better balanced than that of the boys and men of each tribe, and this appeared to be reflected in the differences in their physique and health. The authors in their report admit that causal relationships have not been established between the condition of health and physique and the nature of the diet, but they point out that each dietary is deficient in certain regards. Others have correlated group dietaries with the type of prevalent disease, and have concluded that diets may appear adequate for normal existence, and yet predispose to ailments which are more or less typical for a given dietary. McCarrison's[9] observations are worthy of special note. For many years, studies have been conducted under his direction at the Pasteur Institute, Coonoor, S. India, under environmental conditions which seem ideal for health. Here large groups of rats were fed diets similar to those used by various Indian tribes. The group considered as controls received the diet eaten by the Sikh tribe, members of which are noted for their excellent physique and health; the diet appears adequate in all respects. Various inadequacies existed in the other diets. Each animal was watched throughout its period of life, and after death was dissected and any gross pathology noted. During a period of 28 months there had been no instance of illness among members of the control group, no deaths from natural causes in the adult stock, and aside from a few accidental deaths, no infant mortality. Almost 1200 of the group were subjected to postmortem examination; the only macroscopic evidence of pathology noted was a few instances of tapeworm infestation. Over 2200 animals receiving the poorer diets were subjected to postmortem examination during the same period; these exhibited gross pathologic lesions of diverse nature, embracing almost the whole gamut of human disease, and in marked degree. Correlating these findings with pathologic conditions seen in the human being, McCarrison emphasizes especially the factor of diet in the etiology of goiter, peptic ulcer, and renal calculi, conditions which are common among the tribesmen using the poorer diets.

It is interesting to review the evolution of thought concerning the etiology of dental caries. This, one of the commonest of pathologic conditions, has been accepted until recently as dependent upon the effect of bacteria. About 1890, Miller[10] concluded, after ten years of

study, that dental decay was caused by the action on the tooth of acidic growth products of certain organisms, resulting in decalcification and subsequent destruction of the tooth substance. On the basis of this theory, our whole campaign of oral hygiene has been developed, the public being assured that a clean tooth never decays. Yet teeth that have been kept as clean as practice will permit, have decayed. Various acid-producing organisms found in the mouth have been designated as the specific cause of tooth decay.[11] Until recently, explanations of this type have been accepted unquestioningly by the rank and file of the dental and medical professions. Gradually, however, the concept has spread that the nature of the diet plays no small part in the causation of dental caries. Scientific observations on the effect of food on the teeth were inaugurated by the Mellanbys of England in 1917, and have been continued progressively ever since.[12] Working primarily toward an understanding of rickets, they found that purposely faulty diets fed to laboratory animals gave rise not only to rickets, but also to dystrophy and decay of the teeth. Their premise was verified by other investigators in this country, and in nutritional circles it became an accepted fact that dental decay in animals could be induced by faulty diet. By some students of the problem, this was fitted into previously existing ideas by postulating that diets high in starchy foods would stick to the teeth, and serve as a pabulum for acid-producing organisms. On these grounds, certain dentists have stated that to avoid dental caries, one should avoid starches and sweets, and use food of a fibrous nature so that it would serve to scour from the teeth any sticky débris.[13] This school of thought places emphasis primarily upon the exclusion from the diet of certain types of food. Results of such dietary procedures have led to no consistent lessening of caries. Quite by accident, Boyd and Drain[14] obtained evidence that diets complete in all the recognized essentials would arrest the progress of dental caries in diabetic children. As an outgrowth of this observation, it has been shown[15] and repeatedly confirmed by numerous workers[16] that similar results can be obtained in other children; that a wide variety of diets may be employed as long as all the recognized essentials are included. According to this concept, which is gaining universal acceptance, tooth decay is dependent upon the inadequacy of the diet in certain essentials. These essentials can be supplied entirely by food products (including cod liver oil in that designation) and no foods in themselves are harmful to the teeth. Some workers in this field have attributed caries to some certain specific deficiency, such as vitamin D, vitamin C, or phosphorus. There is much to be said against the acceptance of any of these assumptions as wholly true. The significant fact remains that if a child actually ingests a diet which contains all the elements which are recognized as necessary for health in general, the health of his teeth will be safeguarded as well.

If the incidence of tooth decay can be accepted as an index of the inadequacy of the average American diet, then the importance of dietary supervision becomes established. It emphasizes beyond argument the desirability of change in food habits in many people who may seem to be in good health. In the presence of manifest disease, regardless of its nature, diet supervision becomes more imperative. Langstroth[17] made a clinical evaluation of the home diets of his patients, and from his

data concluded that the American dietary is composed in large measure of concentrated foods, is low in vitamins, residue and alkaline minerals, and high in carbohydrate and acid minerals. According to him, the average diet contains only 12 per cent of the protective foods. Rose[18] states that the three essential diet components most frequently deficient are calcium, iodine and vitamin D. Hopkins, Cathcart, Mellanby and Mottram,[19] appointed to advise the British Ministry of Health on dietary matters, reached similar conclusions, adding vitamins A and C as being potentially deficient in addition to the above; they stated that if the diet were adequate in vitamins D, A and C, probably B vitamin also would be adequate. Sherman[20] has pointed out that the optimal amount of vitamin G probably is much higher than the minimal ("actual") requirement, the difference possibly representing the transition between "passable" and "buoyant" health. He and his coworkers found that the addition of more vitamin G to a diet already adequate resulted in greater growth, development and longevity of their experimental animals. He also concluded that enrichment of the diet in calcium is desirable, and more necessary than is the case with any other mineral. Similarly, the optimum intake of vitamins A and C is considered much in excess of the amount necessary to prevent disease.

Diversity of diet does much to forestall the development of deficiencies; stereotyped menus increase the danger, unless adequate provisions are taken in their formulation. Wilder[21] has called attention to the development of pellagra by patients receiving therapeutic diets for epilepsy, and has stressed the dangers inherent in any prescribed dietary régime in the treatment of disease. Parsons[22] feels that numerous symptoms recognized as characteristic of celiac disease are dependent upon deficiency of ingestion, or of absorption, of necessary food elements. It is known that the infant frequently is subject to manifest deficiency diseases, especially rickets and the anemia of iron deficiency. Clinical scurvy is seen less frequently than was true a generation ago. Mouriquand[23] commenting upon the recognition of subclinical deficiency states in children, describes criteria which he found associated with deficiency of vitamins A, C and D, before the development of clinical keratomalacia, scurvy or rickets, respectively. He states that deficiencies usually are multiple in nature, and that mild deficiencies may be masked if the diet is good in other respects. It is well recognized that the need of the body for protective foods may be greater under some conditions than others. This obviously is true in the case of pregnancy and lactation. The Toveruds[24] have studied the mineral metabolism of women during pregnancy and lactation, and they comment on the marked tendency toward negative balances of calcium and phosphorus during these periods. In some cases they found that a low intake of the necessary factors resulted in breast milk with lowered content of calcium. They concluded that diets poor in calcium, phosphorus and vitamin D during pregnancy and lactation predispose the offspring to rickets and dental caries.

The instances of deficiencies cited in the foregoing deal largely with the dietary factors that were unknown at the beginning of this century. It is quite possible that deficiencies of diet are potentially of much greater significance now than they were a few generations ago, when most foods were eaten without much processing and a variety of foods

was served at each meal. Mendel[25] has contrasted the modern dietary with that of a century ago. The latter offered more in the form of calories, especially as protein foods; the present typical menu contains more dairy products, vegetables and sugar. Higher degrees of refinement of foods, and procedures incident to storage and transportation have done much to rob some of our foods of many of their natural qualities. In another article, Mendel[6] summarizes the recognized essentials of the complete diet as follows: "Researches of the past 20 years have shown that the adequate diet may be regarded as made up of approximately 35 relatively simple substances. Eighteen of these are digestion products of proteins; one, the sugar glucose, is derived either from glucose itself or from cane sugar or milk sugar, starches, etc.; ten are mineral elements (sodium, potassium, calcium, magnesium, chlorine, iodine, phosphorus, sulphur, iron and copper); six are substances designated collectively as vitamins. These are distinguished as vitamins A, B, C, D, E, and G. So far as we now know, any food supply which provides all of these 35 principles in the proper proportions will support normal growth in the young, and maintain health in the adult, provided it contains nothing deleterious." Some of these food factors are designated as "protective foods," thereby implying that care must be taken to include them in the diet in order to avoid deficiency. The remainder are so ubiquitous in their occurrence that little attention need be paid to them other than the provision of satisfying amounts of food of a fairly diverse nature. The current concepts of the occurrence, properties, and medical significance of some of the protective foods will be discussed briefly.

## IODINE

The needs of the body for iodine are definite, but are very small.[26] Von Fellenberg made balance studies of an eight-year-old girl and found that with a daily intake of 38 γ, there was a negative balance of 12 γ. (A γ is a thousandth of a milligram.) He also demonstrated the ability of the body to store larger amounts than needed, if given. Deficiency of iodine intake may result in the development of simple goiter. Seafoods form the richest source of iodine. Foods produced in the areas of the United States where the iodine content of the soil is low will not be valuable sources of this element. Administration of iodine in some form at regular intervals is recommended by many. The form and the relative intervals between administrations seem to be of minor importance.[27] Marine[28] has advised giving from five to ten milligrams weekly, particularly in regions where goiter is endemic. While the measure is one which demonstrably lowers the incidence of goiter in the community, there are reports of occurrence of toxic goiter attributed to the uncontrolled use of iodized salt or other source of iodine. Zimmermann[29] found that 40 per cent of a group of patients with toxic goiter (88 in all) had been taking iodized salt; 67 per cent had been taking some preparation of iodine. He pleads for individualizing the prophylactic administration of iodine. Bleyer and Fischler[30] question the rôle of iodized salt in the production of hyperthyroidism, and suggest that prophylaxis be accomplished by feeding cattle with such a salt. Maurer[31] expresses the belief that prophylaxis through milk of cattle receiving iodized salt has increased safety. If these precautions are necessary one

might expect to find a relative preponderance of toxic goiter on the seacoast, where iodine ingestion is greater than elsewhere. Such an assumption, of course, is contrary to fact.

### IRON

Mackay[32] recently has summarized present views concerning the anemia produced through iron deficiency in the diet, often termed nutritional anemia. She found that in a large series of British infants at a year of age, definite anemia (a lowering of 10 per cent or more below the normal hemoglobin value) was present in 42 per cent of the breast fed, and in 70 per cent of the artificially fed. She stated that the incidence probably was as great in many other countries. The accepted etiology of the condition is a deficiency of iron in the diet, possibly associated with copper deficiency. The fetal storage of iron postpones the appearance of the anemia; in the prematurely born, the storage is less adequate. Milk is poor in iron content, and if it forms the exclusive source of iron for the organism, deficiency is inevitable. Mackay found no evidence of benefit to the child from treating the mother; she advises prophylactic administration of iron ammonium citrate, 1½ grains a day, either added to the feeding or given separately in solution. This should be begun before the infant is 2 months old, or at 1 month in the case of the premature, beginning with smaller doses and increasing gradually. The use of egg as a source of iron is also considered. Josephs[33] concluded that in infants, food iron was less effective than iron-copper preparations in the treatment of these anemias. Elvehjem and Sherman[34] concluded that copper is necessary in the conversion of inorganic iron into hemoglobin.

The danger of iron deficiency lessens as the child's diet becomes more diversified, but it cannot be ignored. Two studies of the iron needs of the preschool child have been reported recently; Rose[35] and her coworkers found their subject to have a negative iron balance with a daily intake of 4.64 mg. Leichsenring and Flor[36] studied the retention of four children between 35 and 56 months of age; these children were all in positive balance, but showed better retention on diets higher in iron. Both groups agree that children of this age require a total of about 8 mg. of iron a day, supplied as iron-containing foods, to insure an adequate margin of safety.

### CALCIUM

The likelihood of dietary calcium deficiency has been expressed editorially as follows[37]: ". . . it becomes highly probable (to speak conservatively) that an unduly large proportion of children who appear, even on careful physical examination, to be making normal growth and development are in reality in a more or less calcium-poor condition simply because their calcium intakes are not high enough to support an optimal rate of calcium retention." Smith,[38] reviewing the effects of malnutrition, stated that growth of experimental animals could proceed during faulty nutrition in a manner which seemed normal in so far as clinical indications are concerned, yet analysis of the bones of such animals showed definite quantitative changes. This is in accord with the observations of Sherman and Booher,[39] who found that when groups of rats were given diets containing graduated amounts of calcium, the calcium content of the bones of the mature animals was proportional

to the calcium intake. They concluded that "the animal body is able to retain calcium at a subnormal rate on relatively calcium-poor diets, and so at an abnormally late age may reach the percentage of body calcium of normal middle-aged adult animals." Milk and milk products are by far the best and safest sources of calcium; it is difficult to supply the postulated daily requirement for children (1 gram) in a utilizable form unless these foods are used freely.[40] The calcium of milk is well utilized by children; the same has been established, in the case of the adult subject, for that of cheddar cheese[42] and for ice cream.[43] The growing organism may not be able to utilize efficiently the calcium from sources which appear adequate for the adult. Sherman studied the effect of substituting half of children's milk allowance with vegetables containing an equivalent amount of calcium, and found that the utilization from the latter source did not equal that from the milk.[41] He states that "vegetables should be used in addition to a liberal allowance of milk and should not be allowed to reduce the amount of milk consumed."

Some pediatricians have expressed the view that if the child is given a quart of milk daily, as recommended by Sherman, the appetite is impaired to such an extent that it is difficult to maintain the desired intake of other foods. The inherent fallacy of this concept need not be discussed in this review. It is of importance in this connection to consider the calcium retentions of children receiving a pint as compared with a quart of milk, as reported by Jeans.[44] On a diet which was adequate in other respects, the retention of calcium on a pint of milk averaged well below the accepted daily requirement; the quart supplied adequate retention.

## THE VITAMINS

At present, six different vitamins are recognized through the clinical effects produced when each is reduced or omitted from the dietary. The vitamin B as described by Funk is recognized now to be a composite of at least two distinct factors; these are known as vitamins B and G in the American nomenclature, as vitamins $B_1$ and $B_2$ by the English. The existence of several other distinct fractions of the vitamin B complex has been claimed by various workers.

The original distinction of vitamins as water-soluble or fat-soluble is emphasized less than formerly: Three are dissolved readily in water (vitamins B, C and G), and three are more soluble in fats (vitamins A, D and E).

Our knowledge of the effects of vitamin deficiency is derived from two varied types of observations. Clinically, evidence of disease has been correlated with the deficiencies of the diet which the patient has been ingesting. Experimentally, healthy animals have been given diets of known composition, deficient in some definite substance or type of foodstuff, and the effect determined by continued observation. It is not surprising that the findings obtained by these two methods do not correlate completely. Conditions have been produced in animals which differ from the syndromes recognized clinically in man; the clinical picture of some deficiency diseases in man has not been duplicated completely in experimental animals. This fact must not be given too much weight. In man, it is unlikely that the diet would be optimum in all respects but one; a deficiency is more likely to be multiple. Like-

wise, deficiency in man will tend to be partial rather than complete, and have a longer time factor than that in animal experiments.

Probably the most outstanding phase of vitamin research during the past few years has been that directed toward determining the nature and the isolation of the individual vitamins. Great strides have been made in this direction. It has been demonstrated that carotene, a plant pigment, is a precursor of vitamin A,[45] and that the liver is able to effect the conversion.[46] Crystalline products have been isolated which, in extremely small dosage, are able to cure beriberi,[47] and which are believed to be the pure antineuritic vitamin.[48] An empirical formula for this substance has been described. A crystalline product which appears identical in properties with vitamin C has been prepared, and has been identified as a hexuronic acid,[49] probably the same substance already prepared from the adrenal cortex, cabbage and other sources of vitamin C.[50] The work of others, identifying vitamin C with the alkaloid narcotine,[51] lacks confirmation. Vitamin D has been obtained in a crystalline form,[52] but it is thought that the product still contains considerable amounts of impurities.

Numerous reviews of the physiologic and clinical aspects of the vitamins have appeared recently in the literature.[45, 53, 54, 55, 56, 57, 58, 59, 60, 61] The discussion which follows has been prepared from these articles and from the reports of the original investigations.

## VITAMIN A

The first evidences of vitamin A deficiency in rats are the loss of subcutaneous tissue, lessened neatness and sleekness, and hoarseness of the voice. All of these precede the development of clinical xerophthalmia. Mouriquand[62] was able to detect alterations in the cornea, a considerable period before the disease was clinically present, through the use of the corneal microscope. The development of night-blindness is recognized as dependent in many instances upon deficit of vitamin A, due to inadequate regeneration of the visual purple.[63, 64] Wolbach and Howe[65] and others have demonstrated that vitamin A is necessary for the normal development and maintenance of the specialized types of epithelial cells. A deficit leads to the loss of ciliation when this is normally present, and eventually to replacement with squamous cells. The resultant drying and loss of cleansing and secreting function play a large part in lessening local resistance to infection. Several studies suggest that vitamin A deficiency lowers the bacterial resistance of the whole body, since animals on diets poor in that factor have been found more susceptible to parenterally induced infections.[66] Whether the anti-infective function of vitamin A can be considered as specific is open to question, since it has been shown that deficiency in other vitamins likewise lowers resistance, and moreover, ill health induced by any measure may be expected to increase the likelihood of infection. The withdrawal of vitamin A results in a varied syndrome, dependent upon the species of animal studied, the degree of inadequacy, the speed of its development, the degree of previous vitamin storage, and the adequacy of the diet in other respects. Among the conditions attributed to its deficiency may be included xerophthalmia, chronic upper respiratory infection, chronic colitis, and calculi of the urinary tract. There is evidence that incidence of upper respiratory infection is not lessened by increasing the vitamin A intake above the amount employed for

prophylaxis against deficiency.[67] Sherman has concluded from studies on rats that deficiency of the diet during the first three years of life may increase susceptibility to upper respiratory infection up to the age of ten to twelve years.[68] Vitamin A can be stored in the body for long periods of time when given in sufficient amounts, thus serving to protect during temporary periods of inadequate ingestion. It is widely distributed in nature, especially in pigmented vegetables (probably present as carotene), in dairy products, eggs, and fish oils. It is quite stable in its sites of natural occurrence, where it is protected from inactivation by antioxidants. Among the good food sources of vitamin A may be mentioned cod liver oil, eggs, butter, liver, carrots, spinach, tomatoes and oranges. The vitamin A content of tomato pulp is 32 times as great as that of the strained juice.[69] Carotene has been proved adequate to protect against deficiency of vitamin A; however, it is readily inactivated by oxidants. Either carotene or vitamin A may be administered orally or parenterally. The interference with growth associated with vitamin A deficiency is recoverable, but may persist.[70] Bloch found no noteworthy residual dental anomaly in children blinded by xerophthalmia. Lane[63] has called attention to the significance of vitamin A deficit to the ophthalmologist, discussing ocular changes which may arise from deficiency of that and of other vitamins. The use of mineral oil may lead to fecal loss of vitamin A from the body in considerable amounts.[71] It is urged that if it is necessary to employ mineral oil frequently, the vitamin A intake be augmented, and the oil be given at a time when intestinal absorption has been completed.[72]

### THE VITAMIN B COMPLEX (VITAMINS B AND G)

Vitamin B, the factor capable of preventing or curing beriberi, is quite readily destroyed by heat. It is necessary for normal growth in the pigeon and rat. Although its deficiency leads to anorexia and subsequent weight loss, these symptoms are not necessarily pathognomonic of such deficiency, since they may arise from other causes as well. Very probably the anorexia is dependent upon the slowing of gastrointestinal movements which characterizes this deficiency. Cowgill[54] feels that subclinical deficiency is quite frequent in this country, as contrasted with the marked rarity of beriberi. Hoobler[73] states that the infant's diet should be supplemented with a potent source of vitamin B. Marks[74] observed clinically a group of patients with constipation, colitis, asthenia, and malnutrition, under administration of supplementary vitamin B as wheat germ, and reported complete relief of symptoms in most cases. In some this was apparent within a few days, while others required six to eight weeks. Others have described the benefit derived by groups of malnourished children from supplemental feedings of this vitamin.[75] On the other hand, there are many authorities who feel that the distribution of vitamin B is so widespread that deficiency of this factor is quite unlikely to arise. Some of the reported benefits from its administration may be explainable on a nonspecific basis. Wheat germ is laxative, aside from its vitamin B content. Many of the functional and pathologic changes reported in animals receiving diets deficient in vitamin B are dependent upon mere inanition; moreover, much of the earlier work in this connection must be revaluated, since it did not distinguish between effects of deficiency of vitamins B and G.

Vitamin G, the heat-stable factor of the vitamin B complex, is termed the anti-pellagric vitamin, although Underhill[56] points out that pellagra may not be a simple deficiency, and that vitamin G deficiency and pellagra are not necessarily synonymous. With marked dietary deficiency of this factor, a considerable latent period may elapse before the appearance of recognizable symptoms. Sherman[20] reported that in rats, some of the first symptoms noted were stunting of growth with diarrhea, or sore mouth, or patchy dermatitis associated with falling hair. On the other hand, he found that adding increased amounts of vitamin G to a diet already adequate, led to increased measure of health, and concludes that the optimum intake is considerably greater than the minimum necessary to prevent disease. Although vitamin G is relatively heat-stable, it does deteriorate at high temperatures and pressures. It does not lend itself to the usual processes of concentration. Sure[55] has suggested that it consists of two fractions, deficiency of the one producing pellagra-like lesions in the rat; inadequacy of the other leading to a decline in growth.

Vitamins B and G have quite a wide distribution; common food sources include milk, lean meat (muscle and solid organs), leafy vegetables and some fruits. Yeast is rich in both factors. Both vitamins are stored in the body if given in sufficient quantity, but not to the extent seen with vitamin A. Sherman[76] states that in general, "there need be no practical danger of shortage of vitamin B except where an unduly large proportion of the calories needed in nutrition are taken in the form of artificially refined foods." Elsewhere, he states that milk is doubtless the most important source of vitamin G in the American dietary.[77]

### VITAMIN C

Wolbach and Howe's work[78] indicates that vitamin C is necessary to bring about the congealing of certain elements in the interstitial fluids, and when it is deficient, a wide variety of pathologic conditions may arise due to the lack of normal cementing action of these elements. Thus, degenerative changes occur in the pulp of teeth very soon after vitamin C is withdrawn from the diet. The fragility of capillary walls is increased. Nerve degeneration may occur. Anemia is of frequent occurrence, possibly as a result of degenerative changes in the bone marrow.[57] In infantile scurvy, the vagus nerve may be affected, explaining the rapidity of the pulse and respiration. The tendency to hemorrhage, separation of the epiphyses and elevation of the periosteum need no comment. Vitamin C is found in various vegetables and fruits; tomato or orange juice is used commonly in the prophylaxis of scurvy, because of the availability, palatability, digestibility, and stability of the vitamin in these foods. Vegetables such as cabbage and lettuce are also valuable sources, if eaten raw. Hess states that, contrary to the current opinion, it is less the acidity of orange and tomato, but rather the anerobiasis, or oxygen potential, that determines the stability of the vitamin. Heating foods in contact with air, especially if in containers of copper or tin, causes rapid destruction of the vitamin C content. It is Hess' belief that the nature of the intestinal flora is of concern in the susceptibility to scurvy, the vitamin deficiency merely predisposing to the disease. It is noteworthy that scurvy is rarely seen since the adoption of orange juice as an essential in the infant's diet. Göthlin[79] has advocated the constrictor test as a means of detecting latent scurvy,

based upon the number of petechiae appearing in a given area at the antecubital fossa within a given time, under defined degree of vasoconstriction. He admits that it is nonspecific, but considers it of value for this purpose. Using it as a guide he concluded that vitamin C deficiency was by no means uncommon in apparently healthy Swedish children, and that the minimum amount of orange juice necessary to maintain normal capillary resistance, in the absence of other source of vitamin C, was 1 c.c. per kilo per day. The animal body does not carry any large store of vitamin C.

### VITAMIN D

This factor is necessary for the normal absorption and utilization of calcium and phosphorus. Its consideration is linked inseparably with that of the calcium and phosphorus content of the diet, not only as to the quantity of each, but their relative proportions. Inadequacy of vitamin D, other factors being optimal, leads to lessened absorption of calcium, as indicated by a diminution of the urinary calcium and an increase of that element in the feces. This in turn interferes with normal bone formation, leading to the development of rickets in the more marked stages of the deficiency, or to subnormal degree of calcification of bones and teeth in deficiency of lesser degree. A disturbance of the normal ratio of serum calcium to the monovalent cations of the blood may result in tetany. Vitamin D is markedly limited in its natural distribution in food. Certan fish oils contain it in abundance, and form a reliable source of supply. Egg yolk contains it in fair amounts, if the hen has had access to vitamin D in quantity. Certain fat derivatives, notably ergosterol, acquire properties characteristic of vitamin D when exposed to ultraviolet rays, either from the sun or from other suitable source. Exposure of the individual to ultraviolet irradiation serves to activate the ergosterol of the skin, thus offering protection against rickets. Many food substances acquire similar properties when exposed to suitable irradiation. In the form that these are marketed, their vitamin D potency is low, as a measure of safety against overdosage. Irradiation merely "converts them from rickets-producing to rickets-preventing foods."[78] It is thought that this is of value especially with cereal foods, since extracts from certain cereals have been found to have rickets-inducing capacity.[80, 81] The danger of clinical rickets is much greater in infants than in older children, largely because of the limitation of the diet and environment of the younger group. The premature infant is especially predisposed to this disease, as he is to other deficiency diseases, because he does not acquire as great a store of calcium and of vitamin D before birth as does the full-term baby. The organism is able to store vitamin D in considerable quantities. As a prophylactic measure, vitamin D should be given daily to the infant from the first few weeks of life, if normal bone and tooth development is to be insured. There is much to recommend, and nothing to contraindicate, its continued administration throughout childhood. The limited distribution of the vitamin makes potential deficiency not unlikely. It is true that sunlight or ultraviolet irradiation may serve as an adequate substitute, yet during certain seasons of the year sunlight may not contribute much to the child who spends the best hours of the day in the schoolroom. It is recommended that vitamins

A and D be administered together since there is need for prophylactic use of each. The consideration in some quarters of viosterol as a substitute for cod liver oil is unfortunate, since viosterol contains no vitamin A. Viosterol has proved of definite value in the prophylaxis and therapy of rickets, but even here its value as compared with cod liver oil has been questioned, since it is reported that cod liver oil appears more effective when given in equivalent dosage.[82] Excessively large doses of viosterol given to animals have caused hypercalcemia, calcium deposits in soft tissues, and death.[83] Such doses are far in excess of the amount advocated for therapeutic use.

### VITAMIN E

This vitamin must be mentioned for the sake of completeness, although up to the present its need by the human being has not been established. In animals its deficiency leads to sterility. The vitamin is found in diverse types of foods; it is highly unstable unless antioxidants are present. Evans[60] has suggested the possibility that the human body may be able to synthesize the substance.

### PRESCRIBING THE DIET

In spite of the apparent complexity of dietary needs, it is not difficult to obtain an adequate diet, using foods which are readily available and reasonably inexpensive. Greater difficulty is encountered in the apathy of the parent, and often of the physician, toward the necessary dietary supervision. The psychic factors in malnutrition are more difficult to meet than are the dietary. It is necessary that the child (and the adult) actually eat the requisite foods, if he is to receive the protection against disease that Nature has furnished.

In all dietary prescriptions, more care is needed to include an adequacy of protective foods than for any other item. During infancy the diet should contain in addition to milk, the following foods, or their equivalent: cod liver oil, orange juice, egg yolk, sieved fruits and vegetables. Certain cereals may be used to advantage, but are less essential than the other foods. Butter, meat, and energy-supplying foods such as bread, cereal, potato, may be added as need arises during the second year. The older child's dietary needs will be met if he takes the following foods daily: one quart of milk, one or two eggs, one teaspoonful cod liver oil, an ounce of butter and an orange or other fresh raw fruit; one fruit in addition; two vegetables, one preferably raw (starchy vegetables are not considered as adequate for this purpose); one serving of meat; starchy foods in amount necessary to make the above diet satisfying. Diets essentially similar to the above have been found capable of arresting dental caries.[15, 16] Other menus, if properly planned, might well accomplish the same end if they included in adequate amount the essentials of a complete diet; yet menus frequently employed in homes and restaurants seem practically devoid of protective factors. In general, the processing of food (milling, drying, canning, etc.), tends to lessen its protective value, in some instances to a marked extent, although with some of the best modern methods such effects are minimized. Some of the foods canned by the present commercial methods retain their vitamin content to a considerable degree; this is less true of foods canned in the home. When "processed" foods

constitute the greater part of the diet, it would be safest to include additional protective foods in amounts sufficient to offset any probable deficiency.

In times of economic stress, the danger of widespread dietary deficiency becomes especially acute. In an attempt to forestall this catastrophe during the present period of depression, various experts in nutrition have prescribed protective measures within the reach of most relief agencies. It is stressed that the child is more likely to suffer at such a time than is the adult, and that group dietaries should be planned with the child in mind. Their advice is available in pamphlet form, and should be used as a guide by each agency administering relief, and in private homes as well.[84, 85] Attention is called to the frequent use of cheap nonprotective foods, when safe diets could be furnished for equal outlay. In a governmental publication[85] prepared under expert supervision, it is recommended that out of every dollar spent for food, one-fourth should go for milk; one-fifth for vegetables; one-fifth for bread, cereals and legumes; one-fifth for starches and sugars, and the remainder (15 cents) for eggs, cheese, meat or fish, and accessory articles. It is urged that every child receive daily at least the following: One pint of milk (he should have 1½ or 2 pints); two teaspoonfuls of cod liver oil (he should have 3 or 4 teaspoons, if diet is not liberal in other protective foods); one vegetable or fruit (he should have three or four); in addition, plenty of bread, cereals, and other energy and body-building foods.

It has been stated recently that six million children of school age in the United States are malnourished.[86] Such a condition is dependent upon ignorance of food needs or lethargy in applying acquired information as much as upon financial stringency. At present the popular magazines and newspapers are devoting much space to advice concerning food. While part of the material is truthful and carefully written, much of it is inspired by food manufacturers or food cultists, with an axe to grind. The physician and his allies must equip themselves to offer authoritative advice in these matters, or the opportunity will pass to those who are less fitted for the task.[87]

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# American Academy of Pediatrics

## Proceedings

### SECOND ANNUAL MEETING OF THE AMERICAN ACADEMY OF PEDIATRICS

FRIDAY AFTERNOON SESSION
May 13, 1932

### Round Table Conference on Allergy

Leader: Dr. Béla Schick; Assistant: Dr. Edwin H. Schorer

BÉLA SCHICK, NEW YORK.—The term "allergy," coined by von Pirquet (ἄλλη,ἔργον), means altered reactivity. The classical examples of allergy were found in the study of serum sickness and vaccination. There is a reaction after the first and succeeding serum injections or implantations of virus in human beings and in animals, but the reaction at the time of the second and subsequent injections or implantations is different in time of onset, as well as in quantity and quality from the first reaction.

The time of onset, called the time of incubation, is shortened with repeated administrations and is eventually reduced to a few hours, minutes, or even seconds. The intensity of the clinical symptoms increases. This increased intensity can become so dangerous that, for example, when experimenting with guinea pigs, death occurs within a few minutes after the intravenous reinjection of horse serum, under symptoms resembling asthma. This peculiar syndrome was called anaphylaxis or anaphylactic shock. It was first discovered in the case of horse serum by Theobald Smith and in the case of actinia poison by Richet. Anaphylaxis is, therefore, only a part of allergy.

Pirquet and Schick tried to explain the mechanism of allergy as follows: Foreign protein or bacterial substances, antigen, injected into or invading the system for the first time, stimulates the development of antibodies, which are digestive in character. These antibodies do not appear until the lapse of from eight to twelve days which is the time of incubation, and they then come into contact with the antigen. The effect of this contact is the formation of toxic substances which are responsible for the symptoms of disease. Such antibodies may still be present when the same antigen is injected or invades for the second time. In this case no incubation time is necessary for the formation of antibodies. Being present, the antibodies can react with the antigen immediately, the toxic substance is instantly formed, and therefore the symptoms of the disease appear shortly after the reinjection or reinvasion of the offending substance. Although other theories have been evolved, our original theory still explains the facts satisfactorily. The cells also participate in the reactions. *Lewis* thinks that an histamine-like substance is formed by the interaction of the antigen and the antibodies. *Dale* suggested that the liver liberates this substance. *Manwaring* points out the importance of the liver in developing the shock. The liver shows signs of damage at the autopsy of animals which suffered

anaphylactic shock. *Manwaring* found that glycogen disappears almost entirely from the dog's liver during the first 15 minutes of an anaphylactic shock.

Allergic symptoms appear in the course of many diseases. Our discussion need not deal with them, but will be confined to the so-called allergic diseases. The symptoms of allergy are so intensive and annoying, even endangering life, that they dominate the situation. Prophylaxis, treatment, and understanding of such diseases are based upon their allergic nature.

The allergic diseases can be classified according to the localization of their symptoms.

A. *Respiratory Tract.* Asthma of different types.

1. Inhalation of emanations of animals, pollen, dust, molds, bacterias, moth, etc.
2. Ingestion of foods or drugs.
3. Influence of physical changes (light, temperature).

*Symptoms* are either fully developed or rudimentary—wheezing, sneezing, coughing, itching sensation in the nose and conjunctiva, vasomotoric coryza (pseudocroup ?), vernal catarrh of the conjunctiva.

B. *Alimentary Tract.* Nausea, vomiting, pylorospasm, enterospasm (colics), diarrhea, colitis, swelling of the tongue, and mucous membrane of the mouth.

C. *Skin* (Ectoderm). Urticaria, lichen urticatus, prurigo, trichophytie, neurodermatitis, dermatitis venenata (occupational), and certain forms of purpura and eczema.

D. *Central Nervous System.* Migraine, certain forms of epilepsy and convulsions. Milder forms show dizziness, headaches, etc.

E. *Circulatory System.* Shock, collapse (especially by intravenous administration), angioneurotic edema.

In the majority of cases the allergic disease localizes in one system only. However multiple localization is not infrequent, and especially eczema and asthma occur in the same individual. It is interesting to note that a relation exists between these two manifestations. In patients suffering from asthma and eczema, the eczema may improve with the onset or increase of asthmatic symptoms and vice versa. The localization of the allergic disease can change. We frequently find that eczema and other skin manifestations in childhood antidate the onset of asthma. It was also found that patients who had suffered from eczema developed migraine, epilepsy, or gastrointestinal forms of allergic diseases.

The etiologic factors enter the organism by the following portals of entry:

(1) Inhalation. (Pollen, animal emanation, house dust, mold)
(2) Ingestion. (Food, drugs)
(3) Infection. (Bacteria)
(4) Injection. (Horse serum, extracts of test substances)
(5) Contact. (Skin, mucous membrane, conjunctiva—involuntarily as, for example, in one's occupation or medically by treating or testing by the scratch or patch test)
(6) Exposure to physical energies. (Change of temperature—heat and cold-, light—sunlight and ultraviolet light)

For making the diagnosis of an allergic disease the following points are of importance:

(1) An exact history, including the occurrence of allergic diseases in the family.
(2) Thorough examination of the patient, including x-ray and testing for tuberculosis.
(3) A visit to the home in order to study the living conditions and food situation.

(4) Testing the patient for the different causes.

Concerning Point 1, the history of the patient, when dealing with children beyond infancy we have to ask especially about the presence of eczema, lichen urticatus during infancy, the occurrence of urticaria after ingestion of certain foodstuffs, and the tolerance especially to milk, eggs, etc. In children with a normal desire for food, a dislike for certain foods is also noteworthy. Sensitiveness to foodstuffs is not always characterized by a skin manifestation, but sometimes by vomiting, nausea, colics, or diarrhea.

We know the influence certain diseases have upon the onset of allergic diseases, so, for example, we find lichen urticatus at times following smallpox-vaccine reaction, and asthma following whooping cough. Sensitiveness to a change in temperature, to colds, to repeated attacks of pneumonia, have also to be noted. The family history often reveals the presence of an allergic disease, either of the same or of a different type in one or more members of the family. All this information must be elicited by questioning, for we cannot expect that such details will be told voluntarily.

*Point 2* concerning the examination of the patient, is self-explanatory.

*Point 3* concerning a visit to the home discloses such facts as to whether or not there are any pets, such as dogs, cats, canaries, etc., and also facts concerning the pillow, bedding, rugs, draperies, furs, etc. The visit also reveals facts concerning the neighborhood, as to whether a stable, garage, or a park with trees and flowers is to be found nearby. This aids in the advice to be given about helpful changes. An investigation concerning the contacts of the child should also be made, as to visits made outside the home as well as concerning visitors who enter the home with especial reference as to whether any dogs, etc., are in this way brought into the home. Finally, it should be learned if the child leaves town for his vacation, and if so whether the new environment influences his condition.

Concerning *Point 4*, testing, for (A) Asthma and Food Allergy, there are the following three forms:

(1) Scratch test
(2) Intracutaneous test
(3) Conjunctival test

We prefer the scratch test. The test material is supplied by commercial houses but in difficult cases the test material must be prepared from the environment itself (house dust, furniture, etc.), in the same manner as the stock test material is prepared.

The use of the intracutaneous test involves a certain amount of danger of a general reaction (constitutional reaction), and we think, therefore, that the scratch test is, for practical purposes, safer. Especially the simultaneous application of several intracutaneous tests can lead to unpleasant anaphylactic symptoms. We use the intracutaneous test in cases where the scratch test is negative and we still suspect that the substance in question may be nevertheless responsible for the allergic disease. In exceptional cases, especially in pollen asthma cases, where the scratch and even the intracutaneous tests show negative results, the application of a dried powder extract directly in the conjunctival sac is advisable. Peshkin has pointed out how important it is to use this form of testing in skin refractory cases of pollen asthma. Before injecting horse serum for therapeutic purposes, the conjunctiva test with powdered serum can also be applied in those cases where the danger of an anaphylactic shock is feared.

In eczema patients the scratch test with the Pirquet instrument (Schloss Moro) and also the intracutaneous method (Woringer) are used. For several years we have been studying the patch test. For this test dry test material is mixed with a drop of 1/10 NaOH, placed on gauze and gutta-percha or cellophan and kept in contact

with the skin over a period of 24 to 48 hours by adhesive plaster. The results with this method of testing are not entirely conclusive as yet. We found several cases of eczema sensitive to feathers (Peck and Salomon). By removal of feathers the eczema cleared up. Moro and Woringer have pointed out the high frequency of positive tests to egg white (over 70 per cent) and the lower frequency to milk (10 per cent). Different forms of allergic dermatitis can be best studied by means of the patch test.

Other tests should also be mentioned.

(1) The Prausnitz Küstner test for passive transfer (direct and indirect-distant)
(2) The Walzer test—injecting the patient with serum intracutaneously and an oral introduction of the substance in question.
(3) The urine proteose test (English authors).
(4) Test by elimination diet (Rowe and Urbach). This method can be used to discover food allergy. New substances are gradually added to the elemination diet, one by one. This procedure can replace, to a certain extent, the scratch and intracutaneous tests.

It must be pointed out that the evaluation of testing is very frequently difficult because multiple sensitization exists. It is not always the strongly positive reaction to a test which proves that that substance is the cause of the allergic disease. Sometimes a slightly positive reaction has more practical importance than the stronger one. Finally in some cases the causative agent has to be found outside the substances usually used for testing.

The testing materials can be divided into several groups:

(1) Inhalants—pollen, etc.
(2) Foodstuffs—meats, eggs, milk, cereals, vegetables, etc.
(3) Bacterial extracts—autogenous and stock vaccines, molds, house dust extracts, etc.

According to our experience (Peshkin) about 80 per cent of the asthma cases given the scratch test show signs of protein sensitiveness; 20 per cent react negatively to the scratch test.

We shall now consider the question of *Therapy*.

*A. Therapy for an Asthmatic Attack.*—Adrenaline solution hypodermically administered (0.1 to 0.5 of a 1:1000 solution) gives relief within a few minutes. After an interval of half an hour the injection may be repeated if the patient is not sufficiently relieved.

In status asthmaticus repeated slow intravenous injections from 0.1 to 0.3 adrenaline have proved to be a life-saving procedure. In this condition, morphine subcutaneously injected is, according to Peshkin and others, contraindicated. We have found that patients refractory to adrenaline treatment improve after removal from their home to the hospital.

Ephedrine has a slower effect and is useful only in mild cases.

Ammonium chloride, sodium iodide in large doses, codein, and other drugs may be used after the acute attack is over.

*B. General Rules for Asthmatic Patients.*—(1) Removal of animals in the household (dogs, cats, birds, etc.). No feather pillows, quilts, or mattresses should be used, and all furs should be avoided. No rugs or hangings should be in the room and the toys should be controlled—none with rabbit hair, etc. The neighborhood should be inspected with reference to stables and garages, and zoological gardens and circuses should not be visited. There should also be no pony riding.

(2) Dietetic restrictions should be observed with reference to the most frequent causes for allergic attacks (egg, fish, wheat cereals, nuts, berries, etc.).

The elimination diets of Rowe may be used.

We give the parents the following two lists of foodstuffs, one containing foods usually found to be harmless, and the other containing foods which should be rather omitted.

*Foods Usually Harmless*

Bread: Rye, whole wheat and graham bread, rolls, toast, plain cookies and cakes, white bread moderately.

Cereals: All kinds, rice, barley and corn flakes.

Eggs: Soft-boiled, coddled and poached.

Milk, butter, cream cheese and light sweet cream.

Beverages: Weak tea, plain malted milk.

Chicken, lamb, beef and squab.

Fish (boiled, broiled or baked): Flounder, trout, sole, weakfish, butterfish, whitefish, pike, karp, perch and bass.

Soup: Chicken and vegetable, purée.

Vegetables: Asparagus, boiled buttered beets, carrots, peas, rhubarb, spinach, string beans, raw cabbage (cole slaw), celery, onion in cooking only, potato, lettuce and tomato. Use lemon with or without olive oil for dressings only.

Fruit: Apple sauce, soft baked apple, cantaloupe, honey dew melon, grapefruit, orange, overripe pear, stewed pear, stewed peach, stewed prune, mashed banana, plum and occasionally pineapple.

Dessert: Jello, custard, tapioca and light puddings.

*Dietetic Restrictions*

Never take iced water, cold water, soda water, celery tonic, beer, ice cream or ice cream soda.

No fried food or pancakes of any kind. No cheese except cream cheese. No cocoa, coffee, chocolate, or sweets of any kind.

No mustard, radish, cucumber, pickles, ketchup, chili sauce, sauerkraut, or delicatessen of any kind.

No herring, gefulte fish, salmon, sardines, smoked fish, bluefish, haddock, halibut, tuna fish, or any kind of shell fish.

No duck, veal, goose, turkey, sweetbread, pork, ham or bacon.

No nuts of any kind. No corn on cob or stewed corn.

No cooked cabbage, cauliflower, eggplant, garlic, lentil, mushrooms, squash, sweet potato, stewed tomato, turnip, broccoli, brussels sprouts. No beans except string beans.

No raw apple, apricot, fig, date, grape, raw peach, raisins, cherry, watermelon, or berries of any kind.

No pies or pastries, hot bread or buns, heavy puddings or jam.

Dinner should be eaten at noon time.

It is important to note that a child can be sensitized in intrauterine life and in infancy during breast feeding through the mother. It is proved that allergens taken by the mother can pass the placenta and can appear in the breast milk. The nutrition of a pregnant or nursing mother has to be regulated.

(3) Protection against sudden changes of temperature: (a) inhalation of cold air, (b) eating ice cold food (ice cream) or drinking ice water, etc.

(4) Avoidance of psychic excitement.

(5) Avoidance of overexertion—no running.

*C. Therapy for the Asthmatic Condition—*

(1) Specific therapy

(a) Avoidance of all substances in accordance with the results of testing. In food allergy the omission of the offending substances for 6 to 12

months is advisable. Frequently we are then able to start with small doses of these substances. The tolerance can be improved.

(b) Desensitization.—Treatment of hay fever and pollen asthma.

1′ Seasonal.

a′ Short and giant ragweed. The treatment should start at the beginning of March or April and continue until the end of September.

| | | |
|---|---|---|
| Solution $\frac{1}{50{,}000}$ | 0.1 c.c.<br>0.2<br>0.3<br>0.4<br>0.5 | Twice a week |
| Solution $\frac{1}{5{,}000}$ | In the same order twice a week | |
| Solution $\frac{1}{500}$ | In the same order twice a week | |
| Solution $\frac{1}{50}$ | 0.06 or 0.07 c.c.<br>0.08<br>0.10<br>0.13<br>0.16<br>0.20<br>0.25<br>0.30<br>0.35<br>0.40<br>0.45<br>0.50 | Twice a week |
| | After 0.50 c.c. is reached this dose is maintained once a week through the pollen season. | |

b′ Mixed grass—Timothy, Red Top, Orchard and June grass. The treatment should start from the middle of January to the middle of February and continue until the fifteenth of July. The treatment is the same as above.

2′ Perennial. The treatment is the same as the preceding and when $\frac{1}{50}$ 0.5 c.c. is reached it is repeated once every two weeks.

(c) Specific Peptons (Propeptan Umbach) taken one-half hour before meals. Excellent results are reported in treatment of lichen urticatus in childhood.

(2) Aspecific Therapy. For this purpose use:

a Milk
b Bacterial vaccine
c Crotalin
d Ketogenic diet
e Pepton

Eventually a and b combined

(a) Milk.

Skimmed milk of poor quality, that is, with many bacteria, is used. The milk is sterilized in an autoclave and ½ per cent phenol is added. The milk is poured into 15 c.c. bottles which can be kept six months.

1′ Treatment with large doses.

An injection is given 3 times a week, starting with ½ c.c., which dose is increased each time by ½ c.c. until 3 c.c. is reached. This dose is then repeated once or twice a week for 3 to 4 more weeks. Longer treatment is useless. The treatment can be repeated after 4 to 6 months.

2′ Treatment with small doses.

An injection of ½ to 1 c.c. is given 3 times a week. This treatment is particularly efficient when combined with vaccine therapy.

(b) Bacterial vaccine.

The vaccine is a mixture of Pneumococci, Staphylococci, Streptococci (hemolytic), Tetragenus, and Friedländer bacillus. It is preferable that the vaccine should be prepared from the sputum of the asthma patient. Commercial vaccines are frequently less effective. Three to four billions bacteria should be in 1 c.c. We can treat with large or small doses as with milk.

1′ Treatment with large doses.

An injection is given twice a week, starting with 0.05 c.c., which dose is increased each time by 0.05 c.c. until 0.5 is reached. This dose is then repeated once a week for 3 to 4 more weeks.

2′ Treatment with small doses.

The original dose of 0.05 c.c. is increased only by 0.01 c.c. and these doses are injected in conjunction with milk twice a week until 0.4 to 0.5 c.c. is reached. Then the injection is made only once a week. If an asthma patient gives a local reaction to the injection, the following dose should not be increased. In the case of a general reaction, adrenaline must be used.

(c) Crotalin—Treatment with snake venom.

The injection has to be done intramuscularly and is somewhat painful. Peshkin uses the venom of Crotalis atrox or horridus, unfiltered, and puts it in a solution composed of 50 per cent glycerin, 50 per cent distilled water, and ½ per cent phenol. One c.c. should contain $\frac{1}{50}$ of a grain of crotalin. For the first injection $\frac{1}{500}$ of a grain is used. Injections are given once a week with a slow increase to a maximum of $\frac{1}{50}$ of a grain. Crotalin is the most efficient substance for producing eosinophilia.

(d) Ketogenic diet (Fineman and Peshkin).

Since the ketogenic diet has a favorable influence in epilepsy, and since certain forms of epilepsy have been explained on an allergic basis, the ketogenic diet can be tried in otherwise refractory cases of asthma. Some of the patients derive benefit. The ketogenic diet apparently influences asthma in several ways; in the first place, by the avoidance of many offending substances which are eliminated automatically as the diet in its strong form contains about 15 gm. carbohydrate, 50 gm. protein, and 180 gm. fat. It has also been suggested by Fineman and Peshkin that the ketogenic diet may have an influence on the physicochemical balance of the entire organism. It is of interest that, contrary to the ketogenic diet, English authors (Oriel) report good results from the administration of high doses of dextrose, giving an additional amount of 1 to 2 ounces in the diet. One dose is given before going to bed and the other in the morning immediately after awaking. This is based upon the observation that the blood sugar figures are low in the morning.

(e) Pepton.

The treatment consisting of the injection of peptons or oral administration did not give as good results as did the other above-mentioned aspecific treatments.

With the idea of making this survey complete, the local treatments used for skin conditions (eczema, etc.) should be mentioned.

Furthermore, we should note the use of allergen-free chambers according to Storm van Leuwen, filters placed in the windows, and masks.

A change of environment is sometimes advantageous for asthma as well as hay fever cases. Peshkin has found that patients with chronic asthma, refractory to all of the aspecific treatments, not only improved after a stay of six to twelve months in the country, but that they could be successfully treated upon their return home.

In spite of all the progress thus far made, quite a number of the children suffering from asthma, 10 to 40 per cent, still remain who cannot as yet be cured, and who have to wait until they outgrow the condition. We hope that this number will gradually decrease as our knowledge of asthma progresses further.

*Question 1.* Difference between Schick, Dick, and tuberculin reactions.

The Schick test is the result of the reaction of the tissues to a primary toxin; i.e., a toxin which acts as such without being altered. Tuberculin is called a "secondary toxin" because it becomes toxic only after contact with substances present in the tissue cells of an individual infected with tuberculosis. The cells are allergic. The Dick toxin shows characteristics of a "primary" and of a "secondary toxin." Dochez called the Dick toxin therefore a toxallergen.

*Question 2.* What is the mechanism of the action of calcium in curing or preventing allergic conditions?

Calcium tightens the spaces between the linings of the endothelial cells of the vessels. In this way it diminishes the amount of exudation. It lowers the excitability of the nervous system (raising the calcium level in the blood serum). Calcium (calcium chloride, calcium gluconate, metaphyllin calcium iodine) may be, therefore, of some value in the prevention of allergic conditions, but is of little value in curing them.

*Question 3.* Does the desensitization produce hypersensitiveness to the same protein?

It occasionally happens.

*Question 4.* Which gives the better results, perennial or seasonal treatment of pollen asthma?

We prefer the seasonal treatment as a regular procedure. It should be remembered that perennial treatment may exhaust the reactivity of the individual.

*Question 5.* What is the value of sulphur treatment in asthma and what is its influence on eosinophilia?

Intramuscular injection of sulphur (suspension in oil) decreases the eosinophilia as a rule. The eosinophilia in the nasal secretion of allergic individuals may be higher or lower in number than in the blood.

*Question 6.* Why are allergic conditions more prevalent in this country than abroad?

Only theories can be made concerning this; for instance, it may be because we have a greater variety of food throughout the entire year in this country and are therefore sensitized to a larger variety of proteins. The air may be infested with a greater amount of different pollens. The concentration of offending pollens may be greater here than abroad.

*Question 7.* What is the relation of allergy to the nervous system?

Allergy is certainly very closely related, especially to the vegetative nervous system. Psychic moments play a great rôle, also the lessened stability of the nervous systems. Therefore for instance, breathing exercises at the beginning of an asthma attack are valuable. The asthmatic patient becomes less frightened and has more confidence in himself.

*Question 8.* How can the fact be explained that a person occasionally wakes up in the middle of the night with an asthmatic attack?

There are different possibilities. In persons sensitive to food, it may be due to the fact that food eaten at the evening meal only reaches the offending phase of digestion several hours later. In persons sensitive to feathers, sleeping on feather pillows brings about the attack during the night.

*Question 9.* Why does the removal of tonsils eventually precipitate asthmatic attacks in allergic children?

The psychic trauma of the operation may be the cause or the actual trauma liberating bacteria or their toxins, which are absorbed.

*Question 10.* In a case of hay fever is it better to desensitize the patient or remove him to a locality free from the offending pollen?

It is certainly better to remove the patient from the source of the offending pollens, but economical or social reasons often prevent such a procedure and therefore desensitization has to be resorted to in the majority of cases.

*Question 11.* How do iodides influence asthma?

It is mostly empirical. It may act by way of the thyroid glands. Second, it liquefies the secretion of the mucous membrane of the bronchi.

*Question 12.* Has any person been permanently cured of asthma by specific injections?

We do not cure asthma, but we improve the tolerance and alleviate the symptoms. The patient may be free from attacks. Children with asthma may lose their attacks.

*Question 13.* Can we always find the cause of asthma in the individual?

The cause of the asthmatic attacks cannot always be found. Improvement may occur without specific treatment. The patient becomes less sensitive.

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# Academy News

## Report of the State of New Jersey by State Chairman

For the furtherance of the White House Conference work, New Jersey held its State Conference on Child Health and Protection at New Brunswick on April 17 and 18, 1931, with an attendance of about two thousand. The Conference was held under the auspices of the New Jersey Conference for Social Work at the request of the Governor of the State. Following the Conference a Continuation Committee was formed to carry out the findings of the Conference. This Continuation Committee directed the respective Chairmen of the four main Sections, namely:

(1) Medical Care
(2) Public Health
(3) Education and Training
(4) The Handicapped

to form their own Committees and translate the findings of their various sections into realities. These findings as to what New Jersey was doing at that time and resolutions for improvement can be found in the two-hundred-page Blue Book, Proceedings of the New Jersey Conference on Child Health and Protection.

These four Chairmen have made progress with their work and a full report of

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Presented at the meeting of State Chairmen, Region I at the Academy of Medicine, New York City.

this progress will be available at the annual meeting of the Continuation Committee at Trenton, New Jersey, on December 2, 1932.

Your present Chairman for New Jersey of the Academy of Pediatrics was the Chairman of Section II, Public Health of the New Jersey Conference on Child Health and Protection. On being given instructions to carry out the findings of the New Jersey Conference as to Public Health matters, I began to form a group of leaders that would eventually link up all of the state, public and private agencies, dealing with child and public health. A Section II Committee was formed which included in its membership Dr. George Palmer, Research Director of the American Child Health Association, a resident of New Jersey and this Committee has already reached many of its objectives. The most important objective of all was, and is, the linking up of child health agencies, in New Jersey for cooperative effort and coordination. The first and most important step toward this was the linking up of the Organized Medical Profession and arousing it to a keen sense of its responsibility in this matter of Child Health. This was done by requesting the New Jersey State Medical Society to appoint a Public Health Committee with the duty of assisting the Public Health Section of the Child Health Conference in prosecuting in New Jersey the findings of the White House Conference. This Committee was appointed in June, 1931 and included in its personnel:

Dr. W. G. Shauffler, Princeton, Chairman, a public health-minded Practitioner,
Dr. Frank Johnson, New Brunswick, a Pediatrician,
Dr. Shapiro, Hudson County, A School Physician,
Dr. Julius Levy, Consultant of the Bureau of Child Hygiene of the New Jersey State Department of Health,
Dr. Allen G. Ireland, Director of Health and Physical Education of the State Department of Public Instruction,
Dr. Stanley Nichols, Asbury Park, New Jersey, Pediatrician.

In this Committee of the State Medical Society, therefore, we have the link-up of

The State Medical Society
The State Board of Health
The State Board of Education

by their official representatives in child health.

This Committee met first in October, 1931 and frequently since, and decided that the first step toward assisting Child Health in New Jersey was to establish working principles as to the relationship of members of the New Jersey State Medical Society to various health agencies.

Six months of effort on the part of this Committee resulted in the submission of the following principles and resolutions to the New Jersey Medical Society at its annual meeting in June, 1932, which were enthusiastically adopted without change or a dissenting vote as the guiding principles of this medical body and its component County Medical Societies in their relationship to health agencies.

Report of the Committee:

The work of the Committee was divided into the following 5 subjects:

I. The State Board of Health, particularly as to the need of full-time health officers.

II. The relationship of physicians to child health activities in the state.

III. The relationship of physicians to school health matters.

IV. The relationship of physicians to hospitals and hospital clinics.

V. The relation and coordination of physicians to health and welfare organizations.

At subsequent meetings of the Committee, detailed reports on these five subjects were received and debated and the following resolutions for presentation to this Society were adopted, and are herewith presented:

### I. STATE HEALTH DEPARTMENT

Resolved that the State Medical Society urgently recommends continuance by the Department of Health of District Health Officers to the full limit allowed, namely 6. (At present only 5 such officers are provided for and, by action of the Appropriation Committee, these will probably be dropped.)

### II. CHILD HEALTH ACTIVITIES

Resolved that:

(1) Physicians should be in attendance at every type of diagnostic or consultation station, whether it be for adults or children.

(2) Physicians should be paid for such work.

(3) Communities should be educated to an understanding that these services are not to replace the private physician and are for those who cannot afford to pay a physician.

(4) This program should be carried out through friendly cooperation with organizations and public health authorities by the Public Health Relations Committee of the State and County Medical Societies.

### III. SCHOOL HEALTH MATTERS

Resolved that:

(1) All school clinics should be discouraged. Immunization against diphtheria; vaccinations; surgical, dental and eye clinics; and any others, should all be discouraged because of the danger or abuse of such clinics, and for the more important reason that such clinics should be relegated to their proper place—the hospital. In rural districts, where there are no clinical facilities, the County Societies should make provision for indigent pupils as may seem most expedient.

(2) All preschool examinations and treatment should be done by the family physician. Immunization against diphtheria and vaccination should be done for all children during the first year of life, since it has been shown that 60 per cent of all cases of diphtheria in children occur before they are 5 years old.

### IV. HOSPITALS AND CLINICS

In view of the special problem created by the increasing number of persons availing themselves of free dispensary and hospital service, who can afford to pay for medical service, and following the recommendation of the American College of Surgeons, that a definite system of determining the social status of the patient in relation to eligibility should be established

Resolved that:

The State Society emphasize the necessity for developing a social service department in connection with every hospital in the State; and, furthermore, that this phase of the work be delegated to the Woman's Auxiliary to the State Society.

### V. HEALTH AND WELFARE ORGANIZATIONS

Regarding the relation and coordination of physicians to health and welfare organizations, the following principles are suggested:

Principle 1. In order to establish a working relationship and coordination between physicians and health and welfare organizations, there must be created state and county committees or councils composed of the executive officials of the state and county medical societies and the executive officials of the health or welfare organizations, with regular meetings to accomplish such coordination.

Principle 2. All public health or welfare work of a medical nature performed by physicians, members of the State Medical Society, shall be on a salary basis except during a limited initial period for demonstration value of such work.

Principle 3. Public or private organizations, and physicians doing health work of any character, shall administer such work so that any person will be assisted in obtaining health facilities in direct proportion to their financial ability to carry their own responsibilities in this respect. A classification shall be made. Suggested classification:

Class 1. Those persons financially able to carry their own responsibilities in regard to health matters.

Class 2. The under-privileged class, receiving less than the living wage and entirely unable to pay for health facilities; persons listed in this class shall receive free treatment at public expense.

Class 3. Those persons who are only partly able to meet their health needs financially during severe or long continued illness or operations. The health needs of this class shall be adjusted by a cooperative plan conceived and directed by the State and County Medical Societies with the assistance of public and private health and welfare agencies.

Principle 4. All administration of these principles shall be with the object of preserving the private relationship between physician and patient.

Principle 5. It is now essential that state and county medical societies assume responsibility for the general health of the citizens of the state of New Jersey and provide means, in cooperation with health and welfare agencies, for the securing of health facilities by all persons regardless of their financial status. If this responsibility is not immediately assumed by our State Medical Society, then political health and welfare agencies will assume—indeed they have already partly assumed—this responsibility, which will inevitably lead to a disruption of the personal and private relationship between physician and patient, and which is the more desirable one for the health needs of the patient.

In view of the above enumerated principles, your Committee recommends the following:

Resolved:

(1) That state and county committees or councils be formed, composed of the executive officials of the state and county medical societies, together with executive officials of the health and welfare organizations, for the purpose of holding regular meetings and of coordinating their work.

(2) That the time has come for the state and county medical societies to assume leadership and responsibility for the general health of the citizens of New Jersey, and thereby preserve the personal and private relationship between physician and patient, which is most desirable for the health needs of the patient.

In presenting this report, your Committee realizes that it has only made a beginning in the study of the questions involved, and respectfully suggests that this study be continued.

This year this Committee is forming a Public Health Committee in each of the 21 County Medical Societies of the State to assist the State Medical Committee in carrying out in each County the child health work of the State Committee. For 1933 this program will be the New Jersey Pre-School Plan. This consists essentially of placing a card (now being designed by Drs. George Palmer and LeRoy Wilkes of the American Child Health Association) in the hands of the mothers of every two-year-old child in the State with the request that:

(1) She have her family physician examine the child twice a year (at his regular office rates).

(2) Record his findings.

(3) Guide the child's health through this period, and that

(4) The mother present the card at school when the child is registered at the age of 5 or 6 as evidence of preparing the child mentally and physically for school. This plan will be

*PROPOSED*

By Section II on Public Health of the New Jersey Conference on Child Health and Protection and the New Jersey Chapter of the American Academy of Pediatrics and

*SPONSORED BY*

The New Jersey State Medical Society officially and carried into effect by the State and County Medical Societies with the assistance of all State and Local Agencies dealing with child health. This latter link-up will be accomplished by the formation of a sub-Committee of Section II of the New Jersey Conference on Child Health and Protection. This sub-Committee will be known as a Child Health Sub-Committee and will be composed of the working officials or executives of all of the New Jersey State agencies, both public and private, dealing with Child Health, such as:

New Jersey State Department of Health
New Jersey State Department of Education
New Jersey State Department of Institutions and Agencies
New Jersey State Department of Labor
New Jersey State Medical Society
New Jersey State Dental Society
New Jersey State Nursing Associations
New Jersey State Parent Teachers Association
New Jersey State Health Officers Association
New Jersey State Child Welfare Division of American Legion
New Jersey State Hospital Association

Also many others too numerous to mention here.

This subcommittee link-up will be used later to put into effect other child health plans formulated by the White House and New Jersey Conferences in a cooperative and coordinated way which is the main need of New Jersey at the present time in the field of Child Health.

When the New Jersey Chapter of the American Academy of Pediatrics is fully recruited, which will take about six months to a year, its Fellows will be appointed on the Public Health Committees in their County Medical Societies and help the State link-up outlined above in carrying out its plans for Child Health. The pediatrician is the logical Public Health leader in Medical Societies and I shall expect every Fellow in the Academy of Pediatrics in New Jersey to lead his County Medical Society in matters of child health and its relationship to County Child Welfare Organizations.

There are about fifty full-time pediatricians in the State who are members of the Medical Society of New Jersey; perhaps a few more not members of the State Medical Society; also an equal number doing largely children's work. We will have twenty-five members enrolled by July 1, 1933.

Means of increasing membership:

(1) Personal work.

(2) A list for each Fellow of the Members of the Academy, so that one Fellow can refer patients to another, thus giving him a reference list of capable pediatricians for his child patients when travelling or moving to other parts of the country.

(3) Dr. Louis Schroeder, Regional Chairman, presented the aims and ideals of

the Academy in the regular program for our Pediatric Section of the New Jersey State Medical Society in Atlantic City in June, 1932.

(4) A meeting of all of the pediatricians of the State will be held at the Newark Academy of Medicine this winter at which a full exposition will be made by various speakers including Dr. S. McC. Hamill, President, and Dr. Louis C. Schroeder, Regional Director of the American Academy of Pediatrics, of the opportunity for pediatricians to meet their responsibilities in child health matters in New Jersey through joining the American Academy of Pediatrics.

The work done by the Academy in Iowa under Dr. Fred Moore has considerable parallel in our own State as follows:

(1) Your Chairman of the Academy presided over the Public Health Section of the New Jersey Conference on Child Health and Protection.

(2) That Section has linked up the Organized State Medical Profession to the Conference and is engaged in linking up all of the other State Child Health Agencies.

(3) The Fellows of the American Academy of Pediatrics in New Jersey are leading members of the Pediatric Section of the State Medical Society and County Medical Society and are the physicians, therefore, who will present and have charge of the pediatric programs and the development of child health activities in the State and County Medical Societies.

The foregoing answers suggest many conditions relating to child welfare that the American Academy of Pediatrics would be interested in and work is going on but one very important condition has not been mentioned, namely the education of the general practitioner in the essentials of pediatric knowledge. This would be the most effective means of promoting Child Health in New Jersey.

The New Jersey State Medical Society in conjunction with Rutgers University Extension Department gives requested short postgraduate courses for any County Medical Society in any subject including pediatrics. This has been a very successful plan but is not wide enough in scope to reach the majority of medical men in New Jersey and give them a working knowledge of pediatrics. We are hoping to create in the several medical schools of New York City and Philadelphia courses in pediatrics to be given on one day of each week for three or six months. Virtually every physician in New Jersey can reach New York or Philadelphia by automobile or train in one to three hours and could take such a course one day a week without disrupting his practice. Such a plan would give every physician in the State a chance to get the essential knowledge of children necessary for everyday care. The object is not to create pediatricians by these courses, but to present present-day pediatric knowledge to the general practitioner. When this comes about, within ten years, instead of having fifty pediatricians and fifty part-time pediatricians in New Jersey, I prophesy that we will have one hundred pediatricians and one thousand part-time pediatricians who will make New Jersey the Child Healthiest State in the Union.

Respectfully submitted,
(Signed) STANLEY NICHOLS.

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Dr. Luther William Holloway, 114 W. Duvale Street, Jacksonville, Florida, has been appointed Chairman of the State Committee of Florida.

Dr. Bernard W. Carey, 660 Frederick Street, Detroit, has been appointed Chairman of the State Committee of Michigan.

The Nominating Committee has submitted the following nominations for Officers for 1933-34: President, Dr. John Ruhrah, Baltimore; Vice-President, Dr. Thomas B. Cooley, Detroit; Chairman of Region III, Dr. Henry Helmholz, Rochester Minnesota to succeed Dr. C. Anderson Aldrich.

# News and Notes

The **American Committee for the International Pediatric Congress,** which meets in London, July 20-23, 1933, together with the **Academy of Pediatrics** and the **Journal,** is arranging a special pediatric trip in connection with the meeting.

In order to keep the expense as low as possible the *S.S. Laconia,* one of the newer 20,000 ton cabin boats of the Cunard Line, has been selected as most nearly fitting in with the needs as regards time and expense. The *Laconia* sails from New York late on the afternoon of July 7, and puts in at Boston on July 8. It then crosses to Liverpool, arriving July 16. The party will then go to London by train or motor and will be accommodated at a hotel convenient to the meetings, and which will be the headquarters of the American delegates and members. On the 23rd of July the group as a party, will break up and each individual will be free to make and carry out his own plans. The minimum rate for passage is $137.00 with accommodations available up to $155.00 (cabins with private baths). If the return is made on a Cunard cabin class boat a discount of 5 per cent is made for the round trip. Frequent return sailings are available from England to New York and Montreal, and the *Franconia* August 12, and *Samaria* August 26 from Havre are available at round-trip rates for those visiting the Continent. Any other line or boat may be used for the return, the Cunard Line being used for the East trip.

The American Express Company Travel Department has been selected as the official agent and all arrangements are to be made through them. The Committee, the Academy, and the Journal accept no responsibility. While sponsoring and arranging for the trip, they will have no part in the details as regards individual arrangements. Mr. Walter C. Gevers of the St. Louis office of the American Express Company, 1010 Locust Street, St. Louis, will have the American end of the trip in charge, and individual arrangements may be made directly through him, or through any office of the American Express Company who will work through Mr. Gevers in arranging reservations as regards this trip.

The American Express Company will be glad to furnish itineraries and make all arrangements for trips and further travel after the meeting, and for the return voyage.

The meeting of the International Association of Preventive Pediatrics will hold its meeting in London just before or after the Congress meets. Details as to hotels, sightseeing, visiting hospitals, etc., during the three days the group will be in London prior to the meeting are being taken up with the London Committee on Arrangements.

The trip will not be limited to members of the Academy and their families, but any physician interested in pediatrics and desiring to make the trip will be welcomed. Further details will be given next month.

# Book Reviews

**Medical Care for the American People.** The Final Report of the Committee on the Costs of Medical Care. University of Chicago Press, Chicago, 1932. Pp. 201.

In November, 1932, the Committee on the Costs of Medical Care submitted this, their final report. From time to time since 1927 reports of many of their studies have appeared and have been read with interest. It is to be regretted that this final report has appeared before the so-called *Summary Volume—The Costs of Medical Care,* Publication No. 27, or certain studies on organized medical service, such as No. 21, as these are referred to in the report as containing certain factual matter which should be available to a reviewer of the final report.

It is not an easy task to review this final report as in itself, it is much in the nature of a review of many studies. Besides this, much of the material is controversial in character and the Committee is far from being unanimous in some of the important recommendations.

The report is an important document. It cannot fail to provoke thought and discussion and any report that does this is worth while. The Committee has made available important data regarding the cost of medical care. If on the other hand, one looks to the report to find a brilliant path of light leading out of the darkness of our medical problems, he is doomed to disappointment. The members of the Committee, men who have given conscientious service for five years, are in sharp disagreement and neither the majority nor minority groups offer a concrete or practical method of solving our difficulties. While in a number of recommendations the committee is quite unanimous, there is nothing in these particular items which could possibly require a five-year study. A group of interested and informed physicians and laymen sitting together for a few hours could frame and agree upon such recommendations as the coordination of medical service, increased emphasis on preventive work in the training of physicians, that the social aspects of medical practice be given greater attention, that specialties be restricted to those especially qualified, or that postgraduate educational opportunities be increased. These and some other of the recommendations as related to nursing education have a familiar ring and are as a matter of fact being carried out at the present time.

That all is not well with the medical world is a recognized fact. It needs no elaborate proof. But this is not a situation peculiar to the field of medicine. Much of the information the Committee has gathered along this line has added detailed knowledge regarding points which every one familiar with the subject knows in a general way. Much of the information thus is interesting rather than important in opening up new ideas or channels of thought.

The first chapter of the Report, entitled, "The Present Status of Medical Care," is devoted to the presentation of certain factual material as the distribution of medical facilities, a study of illness and the costs of medical service among 9,000 white families, the use of preventive medical service, the total costs of medical service, the way in which the medical dollar is spent (physicians receive 29.8c, hospitals 23.4c, and 18.24c is spent for medicines), the distribution of the costs of sickness, professional and institutional incomes, organization, cost of complete medical care, etc. It is all good and interesting reading and is worth re-reading.

Quite wisely the Committee does not try to fix the responsibility for the complexity and unevenness of the present situation, but states in the last paragraph it is a "result of generations of growth."

Chapter II is entitled "The Essentials of a Satisfactory Medical Program." Quite early in this chapter the following statement appears. "No plan is economically sound which does not safeguard quality, since efficient service is in the long run the most economical." No one can disagree with this statement. We quote, as it seems to the reviewer that much of what follows is controversial and hinges about the opinion as to what constitutes efficient service for all the American people and as to whether or not the plans suggested will provide efficient service or will safeguard "quality."

After outlining in detail what the Committee considers a satisfactory medical service, the statement is made that "three major lines of approach are needed."

"(a) The development of types of organized or group practice that will more effectually and economically meet the community's medical needs.

"(b) The distribution, over a period of time and over a group of families or individuals, of the costs of service.

"(c) Provision for the planning and coordination, on a local and regional basis, of all health and medical service."

It is in regard to (a) that the majority and minority groups of the Committee chiefly disagree. More of this later when discussing the "recommendations." Suffice it to say at this time that it is here the reviewer finds the most difficulty. After two careful re-readings of the report he cannot find the factual basis in the report to support the view that organized or group practice will safeguard the quality, emphasized above, and at the same time "more effectively and economically meet the community's needs." In other words we are forced to the conclusion that this approach has its origin in the opinion of some members of the Committee rather than in the factual data or material the Committee has presented. The whole discussion of "service through organized groups" is expository.

The (b) approach involves the question of insurance. We learn that the committee advocates a "voluntary" rather than a "compulsory" form of insurance, despite the fact that it definitely states that in foreign countries the "voluntary" form has had to be made "compulsory" to be satisfactory. It feels that the insurance should be on a non-profit basis (mutual we presume) and that sick benefit insurance should be distinct from insurance for medical service. No figures or even guesses as to the cost of insurance are given.

Approach (c) is a logical deduction from the data in the first chapter.

We feel that in Chapter II the report passes from the realm of fact to that of theory or opinion.

In Chapter III the Committee (majority) "presents its conception of an adequate type of medical organization and an effective method of paying for medical service." "The data in Chapter I shows that many persons are obtaining inadequate medical care at rates which for them are excessive, and that many persons who give this care are receiving inadequate compensation. A remedy lies in the organization of producers and consumers." The first of these two sentences is adequately proved. For the second statement we can find no factual basis in the report and hence we must regard it as an opinion.

The chapter then goes on to outline a theoretical type of organization for cities, for towns and rural areas. The weakness or rather impracticability of the idea is recognized in the statement that "the system outlined may well constitute a goal. . . . Some features are impractical at the moment . . . other features are not feasible immediately . . . essential elements are in the range of practicability."

In brief the plan is chiefly to center about a hospital, all type of medical services. It is unique in that in contradistinction to the type of organization of most existing groups, the family practitioner is to play a rôle which is "prominent and respected." The plan proposed is decidely Utopian in character. The practical objections are easily and pleasantly passed over. As a part of a report our chief objection is that there is nothing presented to show in any way, outside the opinion of the Committee, that such a plan would solve the problems or that such an organization would not in itself bring about a situation in which the muddle of medical service would be increased. One can easily visualize the enormous organization which would be required to put such a scheme into effect. Not one word is given as to what this would cost—and after all is it not this point the committee is studying?

Chapter IV details briefly some of the plans and experiments now under way. Most of these have been developed to meet some local need or condition, as, for example, the health service in connection with colleges. A considerable number of types of organization are discussed which bear very little relation one to another. The minority group believes that only the most favorable examples of "group practice" have been studied.

Chapter V presents the recommendations of the majority of the Committee. The combination of fact with theory of the four previous chapters leads to the *first recommendation* that "medical service . . . should be largely furnished by organized groups. . . . Such groups should be organized preferably around a hospital for rendering complete home, office, and hospital care. The form of organization should encourage the maintenance of high standards and the development or preservation of a personal relation between patient and physician."

The second recommends the extension of all basic public health services.

Recommendation III is to the effect that the costs of medical care be placed on a group payment basis, through the use of insurance.

Recommendation IV urges the coordination of medical services as an important function for every state and local community.

The last recommendation is in relation to the field of medical education.

These in brief and abstract are the recommendations of the majority.

A group of nine members of the Committee present a minority report with certain recommendations of their own. Without discussing these in detail, the chief point of the minority is that they do not consider the idea of the "group" as sound economically, or one that will maintain the high professional standards which they consider the most essential factor. They believe that the restoration of the general practitioner to the central place in medical practice is the soundest and most economical way out of the present situation. They present a number of objections to the "medical center plan." "We look upon this as far fetched and visionary." "It seems to us an illustration of what is almost an obsession with many people, namely, that 'organization' can cure most if not all human ills." But it then in turn recommends "the development by state or county medical societies of plans for medical care." Or by what is commonly called "organized medicine."

It recognizes the present unsatisfactory situation as presented in the data in the first chapter, and "recommends that methods be given careful trial which can rightly be fitted into our present institutions and agencies without interfering with the fundamentals of medical practice." The minority report points out some of the dangers and objections to both voluntary and compulsory insurance. As regards insurance it may be pointed out that neither the majority nor the minority report is unanimous.

If this review is confused or confusing we can only state that it reflects the report. To do the report full justice it would be necessary to quote it almost in its entirety. It is quite clear to the reviewer and will be to the reader that while no practical solution has been reached and that the chief recommendations are

highly controversial and uncertain in their end result, the report is most worth while and valuable. It should and will lead to discussion and thought, and undoubtedly to experiments in medical practice and economics. We see no reason for passing resolutions for or against either the majority or minority reports. It seems quite certain that many changes in the character of "medical service" will take place in the future as they have in the past. We cannot see how any specific program can be laid down in such rapidly changing times as the present. If one could speak definitely of the character of our social structure for even the next ten years, some fairly definite form of a program might be laid down for medicine. Without this it seems rather futile. In fact so many social and economic changes have taken place in the five-year period since the Committee started its work that certain parts or studies seem already out-dated.

The medical profession is an old one—much older than the social sciences—and one that has persisted through many forms of civilization and various types of government. All that we know of the prevention of disease and public health, all the wonderful progress that has been made in the care and treatment of the sick, all hospitals and medical institutions, have originated in the medical profession itself. We are at present in, or have at least been passing through, a commercial age when economic standards have been the yardstick of comparison. We must not be led astray from the high ideals of a profession by an over emphasis of economic or commercial standards.

The report is a valuable presentation of the complexities, troubles and problems of medicine in the present stage of world-wide turmoil. Taken as a whole—including both the majority and minority reports—it presents a fairly complete picture of the situation and suggests remedies to be put into effect. The solution, or rather the final pattern of the changes, will undoubtedly depend more upon the trend of the basic social and economic conditions than upon the remedies as outlined in the report.

BORDEN S. VEEDER.

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**Conferences On Infantile Tuberculosis.** Institute of Clinical Pediatrics and Child Welfare. Director: Professor Luis Morquio, 1932, pages 745.

This volume, the third in a series of major publications appearing from the Institute of Clinical Pediatrics and Child Culture under the direction of the distinguished Latin-American pediatrist Luis Morquio, deals with every phase of childhood tuberculosis. Morquio and a group of distinguished collaborators cover the various topics in the form of conference reports and discuss exhaustively, and with critical appraisal, the present-day knowledge and accepted practice in this field.

The newer conceptions regarding immunity against the disease, and particularly the production of active immunity through such agents as the Calmette-Guerin immunization procedure, receive most extensive consideration and critical evaluation and are the most valuable contributions of this report.

The introductory article by Morquio gives a masterly survey of the entire subject, passing in chronological review all of the great and epoch-making discoveries which have revealed so much of the true etiology and pathology of this disease.

Morquio's critical comments on various procedures of prophylaxis and treatment, brought forward from time to time, are invaluable because they are the fruit of a vast personal clinical experience. He points out that two technical procedures, the cuti-reaction and the x-ray, have probably been the most important factors in advancing our knowledge of the disease and demonstrating its great frequency in the infant and child. This early recognition has led to more effective prophylaxis and treatment.

The mode of infection in childhood tuberculosis is discussed in the light of the author's vast clinical experience. He believes that the infant or child acquires a tuberculous infection only by contact and that the source of infection is almost universally human. He finds that the frequency of tuberculosis increases with the child's age. His statistics for Uruguay show an involvement in the infant under one year of about one per cent, whereas in the child between the ages of eleven and fifteen years, it may reach as high as seventy-five per cent. No age is free from the disease.

The author points out that juvenile or adult tuberculosis is frequently the result of an infection acquired in early childhood, and discusses the factors which cause the juvenile or young adult to fall victim so easily to this disease.

The author favors Ranke's view on the development of tuberculosis and describes fully the three stages into which he divides it, namely the primary infection generally localizing in the pulmonary ganglia and developing allergic reactions leading to calcification; the second stage, or stage of generalized bacillemia and allergic hypersensibility; and the third stage, or localized phthisis accompanied by diminishing allergy, a decreased toxic hypersensibility, and the development of a stage of relative immunity.

The types of tuberculosis seen in infancy and later childhood are grouped according to the scheme and division suggested by Lwesque. In discussing prognosis, the author expresses the view that tuberculosis is curable in the child in the majority of cases, but that such a possibility depends somewhat upon the age, the pathological changes, and the social condition of the subject.

The Calmette-Guerin immunization procedure is discussed favorably. The author is convinced that it is an absolutely harmless procedure and that it confers a manifest resistance to the organism against tuberculous infection.

The treatment of the disease is discussed under the headings of general indications, medicinal therapy, and treatment of localized areas of tuberculosis. Heliotherapy, actinotherapy, radiotherapy, artificial pneumothorax all have their indications. There is no specific treatment of tuberculosis, but all forms must, above all, stress the hygienic and dietetic factors.

Following Morquio's comprehensive review, various special forms of tuberculosis, special symptoms, peculiar pathological conditions, the most approved prophylactic measures, and successful forms of treatment are discussed in minute detail by a group of the leading pediatricians in Uruguay.

The collected presentations form a most complete résumé and critical appraisal of all that is known today about this prevalent disease, and crystallize in authorative opinion what is good and useful in combating this great plague.

The illustrations throughout the book are numerous and are excellent. This is particularly true of radiograph reproductions.

The almost complete absence of bibliographic references is a notable defect in a publication which in all other respects must be classed as a valuable reference work.

Chicago. FRED W. SCHLUTZ.

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**Poliomyelitis.**—A survey made possible by a grant from the International Committee for the Study of Infantile Paralysis organized by Jeremiah Milbank. Williams and Wilkins, 1932, p. 562.

Mr. Milbank with competent advisers has started a new method of approaching the problem of a disease which is even more and more thrusting itself on the public consciousness. His Committee is headed by William H. Park, as chairman, and Josephine B. Neal, as secretary. The other members are the heads of various large laboratories throughout the world. They have financed research workers

and have also had a staff going over the literature of poliomyelitis, now reaching the formidable proportions of over 8,000 titles. From these a bibliography of some forty-three pages has been chosen for the book. The separate chapters are by Miss Elizabeth Hutchins, History; Dr. Helen Harrington, Etiology, Resistance and Immunity and Pathology; Dr. Josephine B. Neal, Symptomatology and Treatment and Dr. Mildred Weeks Wells, Epidemiology.

It is a more ambitious and comprehensive presentation than Dr. Neal's Encephalitis volume which was itself a model of handling the ever growing literature of a subject so that physicians of limited time may familiarize themselves with it.

It is no small feat to digest such a mass of literature and out of it make a readable, easily understood account of such subjects as the neutralizing substances, the immune sera and the like. The summaries of our present-day knowledge of the virus are exceedingly well done, as are the symptomatology and treatment. The addition of a chapter on physiotherapy in its application to poliomyelitis would have been most welcome but the book is limited to the acute stage of the disease.

The chapter on epidemiology is a masterpiece of exposition. Two questions loom large in the public and professional mind; how is it contracted? how can it be cured? Neither can be definitely answered at present, but Miss Wells has given us an account of the possibilities with great clarity. All the possibilities of the first are considered. Transmission by water, given much thought abroad, but little here in America, comes in for consideration and the possibility of an insect vector is also stated. Americans have listened too attentively to statements made too authoritatively that direct contagion is responsible for the disease, and it is high time attention again be given the other possibilities.

The book presents so much material for thought that it is not possible to go into the details. It is a splendid volume which every pediatrist should own and read. It contains everything that has been done up to the present time and is a library on the subject in itself. It is unquestionably the best book on acute poliomyelitis that has yet appeared.

JOHN RUHRÄH.

# Comments

THE final report of the Committee on the Cost of Medical Care, which is reviewed in this number, has already led to considerable discussion and expression of opinion. Discussion and expression of opinion will be welcomed in this column. We have but one stipulation, that comments are based on a reading of the report and not on preformed opinions and prejudices based on reviews and editorials.

THE almost simultaneous appearance of the "Final Report of the Commission on Medical Education," which will be reviewed in next month's issue, is an interesting coincidence. This Commission, of which President Lowell of Harvard is Chairman, was organized in 1925. The first chapter, entitled, "Public Aspects of Medicine," covers much of the same ground as the report of the Committee on Costs of Medical Care, except that it does not attempt to advise a cure. The chapter presents a clear analytical picture of the present situation of the field of medicine. In fact it is a much clearer and more comprehensive picture than that presented by the "Committee on Costs." The report of the "Committee on Costs" appears more in the nature of a special pleading combined with debate, when contrasted with the "Medical Education" report. In connection with the present discussion the following quotations from the latter are pertinent.

"Defects in the methods of medical practice in this country are widely recognized, but there are fundamental advantages in the American scheme which ought to be retained and extended. The solution of the problem is not the destruction of the present system and the substitution of a paternalistic plan ill adapted to the philosophy of American life, but rather the evolution of a pattern which will embrace the desirable features of present methods and the correction of their defects."

"There is some danger that public thinking has been narrowed into an unfortunate position recently in regard to this whole matter, for emphasis is being placed upon the present organization and cost of medical care, rather than upon the support of an adequate medical service of high quality."

"Efforts are made to standardize procedures partly as a reflection of methods in the field of industry. These efforts are based in many instances upon the fundamental fallacy that the human being, who is the unit of medical service, can be regarded as a uniform, standardized organism."

We urge that every physician read these two reports—at least the report of the "Committee on Costs" and the first chapter of the one on "Medical Education." It is not until the clear exposition of the situation in the "Medical Education" report, which presents a keenly analytical and understanding picture of the situation of medicine today, is read, that the chief weakness of the "Committee on Costs" report is seen. Starting out as an excellent study of conditions based on facts, the latter evolves into a rather lively, interesting, and even slightly acrimonious debate among the various members of the committee.

WE WONDER why certain phases of the "Costs of Medical Care" are not referred to more specifically rather than by implication or reading between the lines. Thus, for example, unnecessary hospitalization, the demands for luxurious hospital care rather than necessary hospital care, and unnecessary competition between hospitals which are supported in large part by charity gifts. In the discussion of "group medicine" the fact does not seem to be brought out clearly and

sufficiently that the vast majority of illness requiring medical care does not call for elaborate diagnostic or therapeutic aid. Every practicing physician knows that a part of the costly medical procedures which have come into such routine use are unnecessary and simply pile on the cost.

Is it not true that a large part of the trouble lies with the public rather than the medical profession and present scheme of medical service? Many patients are impressed by "show" in medicine in the same way they are impressed by the elaborate and expensive automobile. The self-selection of specialists, and the jumping around to the latest fad in doctors and therapeutic measures on the part of the patient are not unimportant factors to be reckoned with in the present cost of medical service. The present period of economic distress will probably do more to correct these tendencies than all the reports, studies, and direct efforts that may be suggested.

THAT there is a need for "group" effort and particularly "group" effort to handle at a low cost the small proportion of complicated conditions requiring the interplay of several highly trained specialists is obvious and beyond dispute. This forms, however, but a small proportion of necessary medical service. We have an honest doubt as to the economic and scientific advisability of revamping the organization of the entire medical profession into groups for this reason. The potentialities and probabilities of such a plan leading to or producing conditions more complex and unsatisfactory than the present situation, both to the public and the medical profession, are not theoretical but real.

The basis of medical service has always been an individual personal relationship between physician and patient. The practice of medicine has been perhaps the most individualistic type of work or service that exists. The report recognizes this. One of the chief criticisms of group practice has been that it has had the tendency to break this relationship. Can we be certain that adding the general practitioner to the "group" would preserve this essential relationship?

We hold no brief for or against organization. Many things need and require organization, but there is nothing magical in the word itself. We have been passing through a period where organization has been a fetish of the economic, industrial, and political world. It would be difficult to try and prove today that it has been successful. Some think the only thing necessary is to change the type of organization by introducing radical measures of uncertain end results. Others feel that the wise thing is to correct the defects shown in the present scheme of things and to hold tight to that which is of proved value. Events of the last few years have shown that because a thing is "organized" it is not necessarily sound or even an improvement on the old.